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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES AND EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 001-39450

HARMONY BIOSCIENCES HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**82-2279923**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
630 W. Germantown Pike, Suite 215, Plymouth Meeting, PA	**19462**
(Address of principal executive offices)	(Zip Code)

(484) 539-9800

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.00001 value per share	HRMY	The Nasdaq Stock Market LLC (Nasdaq Global Market)

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, the registrant's common stock was not listed on any exchange or over-the-counter market. The registrant's common stock began trading on The Nasdaq Global Market on August 19, 2020.

As of March 15, 2021, the registrant had 56,891,920 shares of common stock, $0.00001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2021 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2020 are incorporated herein by reference in Part III where indicated.

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Part I

Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, the anticipated impact of the novel coronavirus ("COVID-19") pandemic on our business, business strategy, products, prospective products, product approvals, research and development costs, anticipated timing and likelihood of success of clinical trials, expected timing of the release of clinical trial data, the plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Important factors that could cause such differences include, but are not limited to, statements about:

- our commercialization efforts and strategy for WAKIX;
- the rate and degree of market acceptance and clinical utility of WAKIX, pitolisant in additional indications, if approved, and any other product candidates we may develop or acquire, if approved;
- our research and development plans, including our plans to explore the therapeutic potential of pitolisant in additional indications;
- our ongoing and planned clinical trials;
- our ability to expand the scope of our license agreement with Bioprojet Société Civile de Recherche ("Bioprojet");
- the availability of favorable insurance coverage and reimbursement for WAKIX;
- the impact of the COVID-19 pandemic;
- the timing of, and our ability to obtain, regulatory approvals for pitolisant for other indications as well as any other product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives;
- our commercialization, marketing and manufacturing capabilities and strategy;
- significant competition in our industry;
- our intellectual property position;
- loss or retirement of key members of management;
- failure to successfully execute our growth strategy, including any delays in our planned future growth;
- our failure to maintain effective internal controls; and

- the impact of government laws and regulations.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential”, or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the factors described under the sections in this Annual Report on Form 10-K titled “—Item 1A. Risk Factors.” and “Part II—Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

Unless otherwise indicated, information contained in this Annual Report on Form 10-K concerning our industry, including industry statistics and forecasts, competitive position and the markets in which we operate is based on information from independent industry and research organizations, other third-party sources and management estimates. Management estimates are derived from publicly available information released by independent industry analysts and other third-party sources, as well as data from our internal research, and are based on assumptions made by us upon reviewing such data, and our experience in, and knowledge of, such industry and markets, which we believe to be reasonable. In addition, projections, forecasts, assumptions and estimates of the future performance of the industry in which we operate and our future performance are necessarily subject to uncertainty and risk due to a variety of factors, including those described herein under “—Item 1A. Risk Factors.” and “—Cautionary Note Regarding Forward-Looking Statements.” These and other factors could cause results to differ materially from those expressed and forecasts in the estimates made by the independent parties and by us.

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

As used herein, the terms “Harmony,” “we,” “us,” “our” and “the Company” refer to Harmony Biosciences Holdings, Inc., a Delaware corporation.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. “Risk Factors” in this Annual Report. You should carefully consider these risks and uncertainties when investing in our securities. The principal risks and uncertainties affecting our business include the following:

Risks Related to Our Financial Condition and Capital Requirements

- We have incurred significant losses for most periods since our inception and may never achieve or maintain profitability.
- We have only recently begun generating revenue from product sales and may never be profitable.
- We have a limited operating history and history of commercializing drugs, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We have only limited capital and may need to raise additional capital before we become profitable.

- Raising additional funds by issuing securities may cause dilution to existing shareholders, raising additional funds through debt financings may involve restrictive covenants, and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights to our technologies or product candidates.
- Our auditor has previously expressed substantial doubt about our ability to continue as a going concern and we may be unable to remain a going concern.
- We have made and we may be required to make significant payments in the future to Bioprojet under our licensing and collaboration agreements for pitolisant.

Risks Related to Our Business

- We are substantially dependent on our ability to successfully commercialize WAKIX, which is currently our only approved product. If we are unable to successfully commercialize WAKIX, our ability to generate revenue and our financial condition will be adversely affected.
- The commercial adoption of WAKIX and any other product candidates we develop will depend on the degree of their market acceptance.
- We rely on our license agreement with Bioprojet to provide rights to the core intellectual property relating to pitolisant, and any termination or loss of significant rights under the agreement would adversely affect our development and/or commercialization of pitolisant.
- The ongoing COVID-19 pandemic may result in disruptions to our commercialization, clinical trials, manufacturing and other business operations, which could have a material adverse effect on our business, financial condition, operating results, cash flows and prospects.
- Because a number of companies compete with us, many of which have greater resources that we do, and because we face rapid changes in science in our industry, we cannot be certain that our products will be accepted in the marketplace or capture market share.

Risks Related to Development, Regulatory Approval and Commercialization

- The regulatory approval process of the FDA is costly, lengthy and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for pitolisant in other potential indications for which we may seek to develop pitolisant, our business will be substantially harmed.
- If we fail to obtain and sustain an adequate level of coverage and reimbursement for WAKIX and other product candidates by third-party payors, sales would be adversely affected.
- WAKIX has been approved by the FDA for the treatment of EDS or cataplexy in adult patients with narcolepsy. Regulatory approval is limited by the FDA to the specific indications for which approval has been granted and, unless we seek regulatory approval for additional indications, we will be prohibited from marketing pitolisant for other indications. We may be subject to fines, penalties or injunctions if we are determined to have promoted or be promoting the use of pitolisant for unapproved or “off-label” uses, resulting in damage to our reputation and business.

Risks Related to Our Intellectual Property

- If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.
- If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our current and future product candidates.

Risks Related to Ownership of our Common Stock

- Our directors, officers and principal stockholders beneficially own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

- Future sales of our common stock in the public market, including our directors, officers, or significant shareholders, could cause our share price to fall.

Item 1. Business.

Overview

We are a commercial-stage pharmaceutical company focused on developing and commercializing innovative therapies for patients living with rare neurological disorders who have unmet medical needs. Our product, WAKIX (pitolisant), is a first-in-class molecule with a novel mechanism of action ("MOA") specifically designed to increase histamine signaling in the brain by binding to H_3 receptors. In August 2019, WAKIX was approved by the U.S. Food and Drug Administration (the "FDA") for the treatment of excessive daytime sleepiness ("EDS") in adult patients with narcolepsy, and its U.S. commercial launch was initiated in November 2019. On October 13, 2020, WAKIX was approved by the FDA for the treatment of cataplexy in adult patients with narcolepsy. WAKIX is the first-and-only approved product for patients with narcolepsy that is not scheduled as a controlled substance by the U.S. Drug Enforcement Administration (the "DEA").

We plan to pursue label expansion for WAKIX in narcolepsy in pediatric patients and engage with the FDA in pursuit of pediatric exclusivity. We currently expect to initiate a Phase 3 clinical trial in pediatric patients in the second half of 2021 in pursuit of indications for both EDS and cataplexy. We believe that pitolisant's ability to regulate histamine gives it the potential to provide therapeutic benefit in other rare neurological disorders that are mediated through H_3 receptors and histamine signaling. We are initially focusing on evaluating WAKIX for the treatment of EDS associated with Prader-Willi Syndrome ("PWS") and myotonic dystrophy, otherwise known as dystrophia myotonica ("DM"). In December 2020, we initiated a Phase 2 clinical trial to evaluate pitolisant for the treatment of EDS and other key symptoms in patients with PWS and anticipate topline results in the first half of 2022. In January 2021, we opened an Investigational New Drug application ("IND") for DM and are planning to commence a Phase 2 clinical trial in adult patients with DM1 in the first half of 2021, with topline results expected in the second half of 2022. Beyond these indications, we intend to further explore pitolisant in other rare neurological disorders, potentially including those in which fatigue and cognitive impairment are prominent symptoms with significant impact on daily functioning.

We also seek to expand our pipeline through the acquisition of additional assets that focus on addressing the unmet needs of patients with neurological disorders. We intend to target assets that will be complementary to WAKIX and our expanding list of potential new indications for WAKIX, and assets that will allow us to further leverage the expertise and infrastructure that we have successfully built at Harmony.

Pitolisant was developed by Bioprojet and approved by the European Medicines Agency ("EMA") in 2016 for the treatment of narcolepsy in adult patients with or without cataplexy. We acquired an exclusive license to develop, manufacture and commercialize pitolisant in the United States pursuant to our license agreement with Bioprojet (as amended, the "Bioprojet License Agreement") in July 2017. See "—Strategic Agreement—License and Commercialization Agreement with Bioprojet" for further information regarding the Bioprojet License Agreement. Pitolisant was granted Orphan Drug Designation for the treatment of narcolepsy by the FDA in 2010. It received Breakthrough Therapy designation for the treatment of cataplexy in patients with narcolepsy and Fast Track designation for the treatment of EDS and cataplexy in patients with narcolepsy in April 2018.

Our operating subsidiary, Harmony Biosciences, LLC, was formed in May 2017. We were formed in July 2017 as Harmony Biosciences II, LLC, a Delaware limited liability company, and we converted to a Delaware corporation named Harmony Biosciences II, Inc. in September 2017. In February 2020, we changed our name to Harmony Biosciences Holdings, Inc. Our operations to date have consisted of building and staffing our organization, acquiring the rights to pitolisant, raising capital, opening an IND for pitolisant in narcolepsy, initiating an Expanded

Access Program ("EAP") for pitolisant for appropriate patients in the United States, preparing and submitting our New Drug Application ("NDA") for pitolisant, gaining NDA approval for WAKIX for the treatment of EDS or cataplexy in adult patients with narcolepsy, and launching and commercializing WAKIX in the United States. In addition, we have opened INDs for both PWS and DM and have initiated or intend to initiate clinical development programs in PWS, DM and pediatric narcolepsy to pursue potential new indications for WAKIX.

Initial Public Offering

On August 21, 2020, we completed the initial public offering ("IPO") of our common stock, in which we sold 6,151,162 shares, including 802,325 shares pursuant to the underwriters' over-allotment option. The shares began trading on the Nasdaq Global Market on August 19, 2020. The shares were sold at an IPO price of $24.00 per share for net proceeds of approximately $135.4 million, after deducting underwriting discounts and commissions and offering expenses of approximately $12.2 million. Upon the closing of the IPO, all outstanding shares of our convertible preferred stock were automatically converted into shares of common stock and the accrued dividend payable to holders of the convertible preferred stock was paid out in shares of common stock, resulting in a total of 42,926,630 shares of common stock being issued to former holders of our convertible preferred stock, and warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for a total of 410,239 shares of common stock.

Liquidity and Sources of Funding

For the year ended December 31, 2020, we generated $159.7 million of net product revenues. We have financed our operations primarily with (a) proceeds from sales of our convertible preferred stock, (b) borrowings under (i) our Loan Agreement with CRG and (ii) our Credit Agreement with OrbiMed, and (c) proceeds from our IPO. As of December 31, 2020, we had cash, cash equivalents and restricted cash of $229.4 million and an accumulated deficit of $488.2 million. As of December 31, 2020, we had outstanding debt, net of issuance costs, of $194.3 million.

We believe that our anticipated cash from operating and financing activities and existing cash and cash equivalents will enable us to meet our operational liquidity needs and fund planned investing activities for the next 12 months. We have based this estimate on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we expect. See "Part II—Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources."

Our revenues and expenses in future quarters may differ from our expectations as we:

- commercialize WAKIX in the United States for the treatment of EDS or cataplexy in adult patients with narcolepsy;
- incur sales and marketing costs to support the commercialization of WAKIX and any additional product candidates;
- pay royalties and make milestone payments to Bioprojet for the license of WAKIX;
- incur manufacturing costs for WAKIX and any additional product candidates;
- implement post-approval requirements related to WAKIX;
- conduct clinical trials in PWS, DM and potential new indications for pitolisant or any additional product candidates;
- conduct a pediatric narcolepsy program in pursuit of an indication and extension of our patents based on pediatric exclusivity;
- conduct earlier stage research and development activities for pitolisant;
- support independent investigator-initiated research for which there is a valid scientific rationale;

- hire additional personnel;
- invest in measures to protect and expand our intellectual property;
- incur interest expenses in conjunction with our debt facility;
- seek regulatory approvals for pitolisant or any additional product candidates that successfully complete clinical development;
- acquire certain ex-U.S. rights for WAKIX from Bioprojet and subsequently seek foreign regulatory approvals for WAKIX in certain of those jurisdictions;
- acquire or in-license additional assets; and
- incur additional costs associated with being a public company.

Commercial Launch Metrics

As of December 31, 2020, over 2,400 unique healthcare professionals ("HCPs") (out of a total of approximately 8,000 HCPs who treat approximately 90% of diagnosed narcolepsy patients) have prescribed WAKIX since it became available in November 2019. The average number of patients on WAKIX at the end of 2020 was approximately 2,500. We have secured formulary access for approximately 80% of all insured lives (Commercial, Medicare and Medicaid) in the United States. Within these covered lives, we have observed favorable access to WAKIX subsequent to the expanded approval of WAKIX for the treatment of cataplexy in adult patients with narcolepsy in October 2020.

COVID-19 Business Update

With the global impact of the COVID-19 pandemic, we have developed a response strategy that includes establishing cross-functional response teams and implementing business continuity plans to manage the impact of the pandemic on our employees, patients, HCPs, and our business.

Despite our response strategy, the COVID-19 pandemic is having an effect on our business and the pharmaceutical industry in general, and is impacting the way stakeholders interact with one another during this pandemic. We continue to leverage technology and virtual engagement initiatives to offset our reduced in-person access to HCPs. The COVID-19 pandemic, which has led to high unemployment and corresponding loss of medical insurance, has caused a change in relationship dynamics between patients and their HCPs and has impacted the way patients take, or do not take, their medication. Based on these factors, we expect that the revenue growth rate in future quarters may be adversely impacted by the ongoing COVID-19 pandemic.

We continue to identify new and innovative ways to maintain meaningful engagement, generate awareness and educate our patients, HCPs and payors to minimize the pressure from the COVID-19 pandemic on our business and support our commercial launch performance.

Commercialization

With respect to our commercialization activities, we believe the COVID-19 pandemic is putting pressure on top-line prescription demand for WAKIX, primarily due to (i) our field sales team's reduced ability to access HCPs in person, and (ii) fewer patients seeing HCPs for prescriptions or treatments. The impact on demand for WAKIX may also be related to a reduced ability of prescribers to diagnose narcolepsy patients given the limitations in access to sleep testing, the reduced ability to see patients due to (i) cancelled appointments and (ii) the reprioritization of healthcare resources toward the treatment of COVID-19, both of which lead to fewer prescriptions. Despite these challenges, we continue to engage and educate HCPs virtually on the overall benefit/risk profile of WAKIX and continue to provide support for people living with narcolepsy. As offices, clinics and institutions have begun to allow limited in-person interactions pursuant to health authority and local government guidelines, our field teams continue to re-initiate in-person interactions with HCPs and customers, but the timing

and level of engagement vary by account and region and may be adversely impacted in the future where reemergence or future outbreaks of COVID-19 may occur.

High unemployment and the corresponding loss of health insurance is causing some eligible patients to shift from commercial insurance to free goods and patient assistance programs, which impacts our ability to convert demand to revenue. Depending on the scale and ultimate duration of the COVID-19 pandemic and the extent of an economic slowdown, widespread unemployment and resulting loss of employer-sponsored insurance coverage, we may experience a shift from commercial payor coverage to government payor coverage or continued/increased demand for patient assistance and/or free drug programs, which could further impact our net revenue in the coming quarters.

Supply Chain

We currently expect to have adequate supply of WAKIX through the first half of 2022, with additional API on-hand inventory to support 12 to 18 months beyond this time frame. We are working closely with our third-party manufacturers, distributors and other partners to manage our supply chain activities and mitigate potential disruptions to our product supplies as a result of the COVID-19 pandemic. We believe that our access to the required production lines to produce additional API and WAKIX finished product throughout the next 12-18 months will not be directly impacted by the potential need to reprioritize manufacturing resources due to the production of materials utilized for COVID-19 vaccines.

Our manufacturing partners in France and the United States continue to be operational. If the COVID-19 pandemic persists for an extended period of time and/or begins to impact essential distribution systems such as transatlantic freight, FedEx, UPS and postal delivery, we could experience disruptions to our supply chain and operations with associated delays in the manufacturing and supply of our products.

Research and Development

The COVID-19 pandemic has negatively impacted the pharmaceutical industry's ability to conduct clinical trials. While we initially experienced some challenges due to the COVID-19 pandemic, we have taken measures and put contingency plans in place in order to advance our clinical development programs. We have implemented remote and virtual approaches to clinical trials, including using telemedicine for remote clinic visits to perform efficacy assessments and sending out licensed HCPs to each patient to collect safety assessments (e.g. labs, electrocardiograms) as required by the protocols. We are also performing remote site visits and data monitoring where possible. These measures are being instituted with the intent of maintaining patient safety and trial continuity while preserving study integrity. One unique challenge we are facing is the ability to access sleep labs during the COVID-19 pandemic in order to conduct objective sleep testing, which is required for some of our clinical trials. In addition, we rely on contract research organizations ("CROs") or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. If the COVID-19 pandemic continues and persists for an extended period of time, or reemerges in the future, we could experience significant delays in our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Corporate Development and Other Financial Impacts

The COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of domestic and global financial markets. If the disruption persists and/or worsens, we may be unable to access additional capital, which could negatively affect our ability to execute on certain corporate development transactions or other important investment opportunities. The pandemic could also impact our ability to conduct in-person due diligence, negotiations, and other interactions to identify new opportunities.

The COVID-19 pandemic has also affected, and continues to affect, our business operations and financial results. The extent of the impact of the COVID-19 pandemic on our ability to generate sales of, and revenues from, our approved products, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of or reemergence of outbreaks,

governmental travel restrictions, quarantines, social distancing and business closure requirements in the United States, France, and other countries, and the effectiveness of actions taken globally to contain and treat COVID-19.

Corporate Responsibility Impact

We continue to provide support to our local communities, patient-focused organizations and other charitable organizations during the COVID-19 pandemic with relief efforts, including corporate donations, supplying food, medical supplies and other resources. For the safety and well-being of our employees, consultants and their families, during the COVID-19 pandemic, we have abided by government-issued work from home orders. We continue to clean and sanitize our offices on a regular basis and have implemented COVID-19 screening procedures and social distancing guidelines before allowing employees or guests to enter our offices.

Narcolepsy Market Overview

Narcolepsy is a rare, chronic and debilitating neurological disorder of sleep-wake state instability that is estimated to affect approximately 165,000 Americans, with fewer than 50% diagnosed. Narcolepsy is characterized by EDS, which is present in all patients with narcolepsy and is the primary reason why patients seek treatment. EDS is the inability to stay awake or alert throughout the day, including an irrepressible need for sleep, with lapses into drowsiness or sleep, which has a significant impact on a patient's ability to function. Additional symptoms of narcolepsy may include cataplexy (which is characterized by sudden and transient episodes of muscle weakness accompanied by full conscious awareness), hallucinations, sleep paralysis and disrupted nighttime sleep. In most patients, narcolepsy is caused by the loss of hypocretin, a neuropeptide in the brain that, along with histamine, works to support sleep-wake state stability. This disorder affects men and women equally, with typical symptom onset in adolescence or young adulthood; however, it can take up to a decade after onset of symptoms to be properly diagnosed. The U.S. narcolepsy market had an approximate net sales value of $2.1 billion in 2020. The market is expected to continue to grow based on several factors, including, but not limited to, the introduction of new innovative therapies that offer novel mechanisms of action resulting in improved safety/tolerability profiles while delivering clinically meaningful efficacy, additional investment in education, increased rates of diagnosis, and population growth.

Prior to the FDA's approval of WAKIX in 2019, there were six approved medications to treat patients with narcolepsy, all of which are scheduled as controlled substances, and no new therapies had been approved for narcolepsy patients in the United States since 2007. These medications include Xyrem (sodium oxybate), Provigil (modafinil), Nuvigil (armodafinil), Ritalin (methylphenidate), Adderall (amphetamine salts) and Sunosi (solriamfetol). Following the approval of WAKIX, in July 2020 the FDA approved a new lower sodium formulation of Xyrem (Xywav). These approved drugs are prescribed in accordance with their individual labels for indications covering narcolepsy, cataplexy and/or EDS related to narcolepsy, and have demonstrated the ability to improve the lives of the patients suffering from these symptoms. Other prescription drugs are used off-label for the treatment of either EDS or cataplexy in patients with narcolepsy, including stimulants for EDS and antidepressants for cataplexy. Despite the benefits provided by the available medications, according to the American Academy of Sleep Medicine ("AASM"), traditional stimulants, wake-promoting agents and sodium oxybate, at best, provide only moderate improvement in narcolepsy symptoms and side effects may limit their use. Some of the current therapies have significant side effects (such as increased heart rate and blood pressure) and boxed warnings due to the risk of respiratory depression, abuse and dependence. These therapies also have the potential for rebound and withdrawal symptoms. The Voice of the Patient report from the FDA's patient-focused drug development initiative, published in 2014, concluded that, based on the overall benefit-risk assessment of current medications, there is a continued need for additional effective and tolerable treatment options for patients with narcolepsy. In a retrospective electronic chart review conducted by Rush University Medical Center from June 2011 to December 2018, over 75% (73 out of 97 respondents) of patients with narcolepsy reported at least one residual symptom while on their current treatment. In a third party survey that we commissioned prior to the commercialization of WAKIX, of the 200 patients with narcolepsy who were surveyed, 86% (173 out of 200 respondents) of patients reported narcolepsy is a life changing disorder and 93% (157 out of 169 respondents) expressed frustration with current treatment options, while 31 patients were not on treatment and, as such, did not provide a response to this question. The main drivers of patients' dissatisfaction were side effects and tolerability, loss of efficacy over time and concerns about abuse and dependence with current therapies.

In market research sponsored by us prior to the commercial release of WAKIX, both patients and healthcare professionals ("HCPs") expressed frustration and dissatisfaction with then-existing therapies, reflecting current unmet medical needs. These unmet needs included, in order of importance, the availability of: (i) non-scheduled treatment options, (ii) more tolerable treatment regimens, (iii) more effective treatment options, (iv) novel MOAs beyond currently available therapies and (v) once-daily treatment options. Based on our market research, we believe the most significant unmet need identified was the availability of non-scheduled treatment options. Other than WAKIX, all drugs approved by the FDA for the treatment of narcolepsy, including stimulants, are scheduled as controlled substances by the DEA. Controlled substances have the potential for abuse, misuse, and diversion. In addition, these products also have the potential for the development of tolerance and withdrawal symptoms. Despite their inherent drawbacks, due to the limited number of treatment options, stimulants have historically been a primary treatment for people with narcolepsy. In addition to having the potential for abuse, all of the treatments approved for narcolepsy, except WAKIX, require a Risk Evaluation and Mitigation Strategy ("REMS") program, which is required by the FDA for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.

Our Solution

WAKIX (pitolisant) represents a novel approach to narcolepsy treatment. We believe that WAKIX offers a meaningfully differentiated product profile over current treatment options for the following reasons:

- ***First-in-class molecule with a novel MOA***. WAKIX is the only selective H_3 receptor antagonist/inverse agonist approved by the FDA. It is approved for the treatment of EDS or cataplexy in adult patients with narcolepsy and is the only narcolepsy treatment that works primarily through histamine, a major wake-promoting neurotransmitter. Pitolisant is thought to work by regulating histamine, such that it activates wake-promoting neurons and inhibits sleep promoting neurons, which helps to stabilize states of sleep and wakefulness. We believe that these novel characteristics differentiate it from other narcolepsy treatments.

- ***First-and-only non-scheduled treatment for narcolepsy***. WAKIX is the first-and-only FDA-approved treatment for narcolepsy that is not scheduled as a controlled substance by the DEA. We believe one of the most significant unmet needs is the availability of non-scheduled treatment options. In a clinical trial, pitolisant demonstrated statistically significantly lower drug liking compared to phentermine (a Schedule IV stimulant), consistent with its lack of abuse potential.

- ***WAKIX is not a stimulant***. Stimulants are one of the most commonly prescribed treatments for patients with narcolepsy. Unlike stimulants, in clinical trials, WAKIX has shown no evidence for the development of drug tolerance or withdrawal symptoms. Therefore, there is no need for patients to temporarily stop the medication to reset efficacy. In addition, unlike stimulants, WAKIX does not increase dopamine levels in the brain's reward center, which contributes to its lack of abuse potential. According to the National Sleep Foundation, stimulants have the potential for abuse, so their use must be considered carefully by patients and HCPs. WAKIX gives patients and HCPs a different therapeutic option.

- ***WAKIX can be used as monotherapy or administered concomitantly with other narcolepsy treatments***. Narcolepsy is a difficult disorder to manage and the majority of narcolepsy patients often require multiple medications to treat their symptoms. WAKIX was studied in combination with each of modafinil and sodium oxybate (two common treatments for narcolepsy) and demonstrated no effect on the pharmacokinetic ("PK") profile of either treatment, and neither treatment had a clinically relevant effect on the PK profile of WAKIX. We believe the ability of WAKIX to be taken as monotherapy or concomitantly with other narcolepsy medications affords HCPs the flexibility to better manage their patients with narcolepsy.

- ***WAKIX is a once-daily oral tablet administered in the morning upon wakening***. Patients have identified a need for treatment options that are easier to take and are dosed less frequently. We believe that once-daily dosing with WAKIX addresses this need and may help improve patient compliance with treatment.

Our Strategy

Our goal is to become a leading pharmaceutical company dedicated to developing and commercializing novel treatment options for patients living with rare neurological disorders who have unmet medical needs, beginning with a focus on narcolepsy. The key elements of our strategy are outlined in our three pillars of growth:

- Pillar I: Optimize the Commercialization of WAKIX in Adult Patients with Narcolepsy

    - ***Commercialize WAKIX in the United States***. We have assembled a team of approximately 150 professionals that possess comprehensive life sciences experience. We have also established a robust company infrastructure to execute on our core business and growth strategies. This team includes over 70 dedicated and experienced sales professionals who call on the approximately 8,000 HCPs who treat approximately 90% of narcolepsy patients in the United States. In November 2019, we launched commercial sales of WAKIX in the United States.

- Pillar II: Expand the Clinical Utility of WAKIX

    - ***Expand WAKIX Label in Narcolepsy***. Building upon the EDS and cataplexy indications in adult patients with narcolepsy, we expect to initiate a Phase 3 clinical trial in pediatric narcolepsy patients in the second half of 2021 with the goal of gaining a pediatric indication for both EDS and cataplexy. We also plan to engage with the FDA to pursue pediatric exclusivity.

    - ***Pursue New Indications Beyond Narcolepsy***. We believe that pitolisant's novel MOA offers a *portfolio in a product* opportunity and has therapeutic potential in several other patient populations with rare neurological disorders. We submitted an IND for PWS in October 2019 and received acknowledgement from the FDA that the proposed clinical investigation may proceed. We subsequently completed a Phase 1 PK clinical trial in pediatric patients with PWS in the fourth quarter of 2019, and initiated a long-term, open-label safety trial in these patients. In December 2020, we initiated a Phase 2 clinical trial to evaluate pitolisant for the treatment of EDS and other key symptoms in patients with PWS, including behavioral symptoms and cognitive impairment. Topline results from this clinical trial are expected in the first half of 2022. For patients with DM, we are planning to evaluate pitolisant for the treatment of EDS and other key symptoms, including fatigue and cognitive impairment. We submitted an IND for DM at the end of 2020 and the IND opened in January 2021, after which we received a "Study May Proceed" letter from the FDA in February 2021. We plan to initiate a Phase 2 clinical trial in patients with DM1 during the first half of 2021 and anticipate topline results in the second half of 2022. We also plan to explore pitolisant's potential as a treatment for EDS and related symptoms in other rare neurological disorders, potentially including those in which fatigue and cognitive impairment are prominent symptoms with significant impact on daily functioning.

- Pillar III: Acquire New Assets to Expand our Product Portfolio

    - ***Explore Expansion of our Product Portfolio***. As we continue our commercial growth and the advancement of our clinical development programs with pitolisant, a key component of our strategy will be to expand our product portfolio beyond pitolisant by partnering, co-developing or acquiring assets focused on rare neurological disorders and/or other disorders with unmet medical needs that are complementary to our existing research and development expertise and/or commercial footprint.

Our History

Our operating subsidiary, Harmony Biosciences, LLC, was formed in May 2017. We were formed in July 2017 as Harmony Biosciences II, LLC, a Delaware limited liability company, and we converted to a Delaware corporation named Harmony Biosciences II, Inc. in September 2017. In February 2020, we changed our name to Harmony Biosciences Holdings, Inc.

Since inception, we have raised approximately $493 million in equity financing. We have assembled an experienced leadership team with a track record of developing and commercializing products to treat rare neurological disorders. We believe that the clinical development, regulatory, commercial, and operational expertise of our executive and senior leadership team will be essential as we execute on our strategy of becoming a leading pharmaceutical company focused on developing and commercializing innovative therapies for the treatment of rare neurological disorders while delivering significant value to both patients and shareholders.

Overview of Development Pipeline

Label Expansion

While all patients with narcolepsy have the primary symptom of EDS, for which WAKIX was originally approved in adult patients, it is estimated that 60% to 70% of those diagnosed with narcolepsy and treated also experience cataplexy, representing approximately 25,000 to 30,000 patients in the United States. On October 13, 2020, we received regulatory approval for WAKIX for the treatment of cataplexy in adult patients with narcolepsy. We believe that the additional indication for cataplexy in adult patients strengthens the product profile of WAKIX and helps to facilitate access to WAKIX for adult patients suffering from both EDS and cataplexy associated with narcolepsy.

We are actively working on our goal of label expansion for WAKIX in narcolepsy by pursuing an indication for pediatric patients suffering from narcolepsy. Approximately 3,600 of the diagnosed narcolepsy patients in the United States are 19 years of age or under. We believe that pediatric patients could benefit from new treatment options. Accordingly, we currently expect to initiate a Phase 3 clinical trial in the second half of 2021 for indications of both EDS and cataplexy in pediatric patients. Topline results from this clinical trial are expected in the first half of 2023. We also intend to submit a Pediatric Written Request to the FDA with the goal of obtaining pediatric exclusivity.

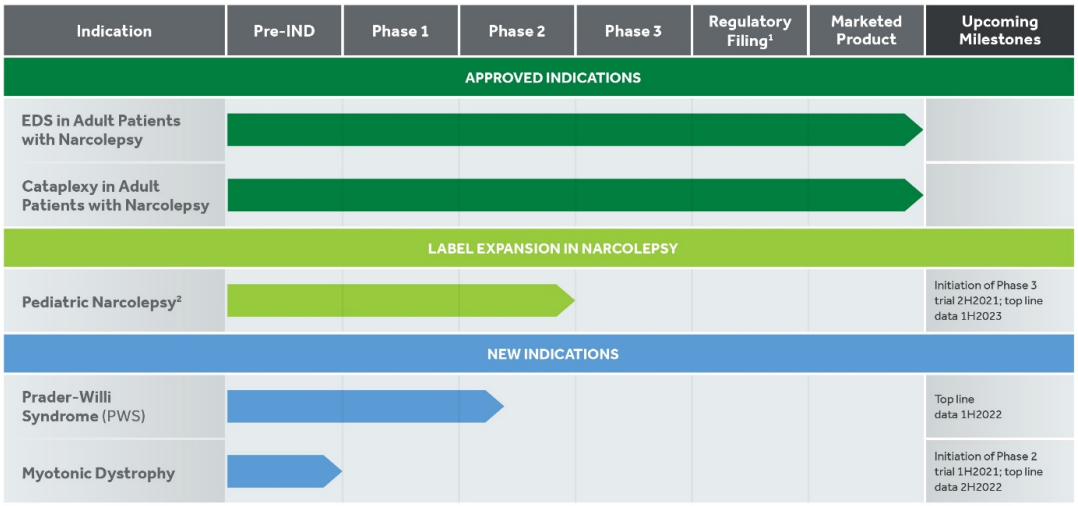
Additional Indications

We believe that pitolisant's ability to regulate histamine gives it the potential to provide therapeutic benefit in other rare neurological disorders that are mediated through the H_3 receptor and histamine signaling and offers a *portfolio in a product* opportunity with pitolisant. We plan to explore the potential benefit of pitolisant in additional rare neurological indications beyond narcolepsy, initially focusing on the treatment of EDS associated with PWS and DM.

PWS is a rare genetic disorder caused by a loss of function of specific genes on chromosome 15 resulting in hypothalamic dysfunction. The hypothalamus controls both sleep-wake states and hunger-satiety. Therefore, two of the main symptoms in patients with PWS are EDS and insatiable hunger, or hyperphagia. Other consequences of PWS include low muscle tone, short stature, behavioral problems and cognitive impairment. It is estimated that approximately 15,000 to 20,000 people in the United States suffer from PWS, and over half of those suffering from PWS also have reported or experienced EDS, for which there are no FDA-approved treatments. We completed a Phase 1 PK clinical trial in the United States in pediatric patients with PWS in the fourth quarter of 2019, and initiated a long-term, open-label safety study in these patients. In December 2020, we initiated a Phase 2 clinical trial in patients with PWS and anticipate topline results from this clinical trial in the first half of 2022.

DM is a rare, multi-system genetic disease that affects the neuromuscular system as well as several other systems, for which there are no FDA-approved treatments. It is inherited in an autosomal dominant pattern and there are two main types: type 1 ("DM1") and type 2 ("DM2"). The underlying cause of DM1 is a mutation in the myotonic dystrophy protein kinase ("DMPK") gene on chromosome 19. DM1 is the most common form of adult-onset muscular dystrophy and affects as many as 140,000 patients in the United States. EDS and fatigue are hallmark clinical characteristics in the majority of patients with DM1 and are referred to as the most frequent non-muscular symptoms in patients with DM1. Cognitive impairment is also a prominent symptom in patients with DM1 and all of these symptoms are thought to be mediated through H_3 receptors and histaminergic pathways located throughout the central nervous system ("CNS"). DM2 is not as common as DM1 with an estimated prevalence of between 3,000 and 29,000 patients in the United States. The underlying cause of DM2 is a mutation in the CCHC-Type Zinc Finger Nucleic Acid Binding Protein ("CBNP") gene on chromosome 3. Patients with DM1 and DM2 share similar phenotypes but disease onset is later in patients with DM2 and symptoms tend to be milder. We submitted an IND for DM at the end of 2020 and the IND opened in January 2021, after which we received a "Study May Proceed" letter from the FDA in February 2021. We plan to initiate a Phase 2 clinical trial in patients with DM1 during the first half of 2021 and anticipate topline results from this clinical trial in the second half of 2022.

Development Pipeline Chart



1. Includes New Drug Applications and supplemental New Drug Applications.
2. Current trial being conducted by Bioprojet. We plan to initiate a Phase 3 clinical trial in 2H2021 in pursuit of pediatric indications for both EDS and cataplexy as well as pediatric exclusivity.

Beyond the target indications listed above, we believe there are opportunities related to CNS disorders of hypersomnolence that we may pursue. We also intend to further explore pitolisant in other rare neurological disorders, potentially in those in which fatigue and cognitive impairment are prominent symptoms with significant impact on daily functioning. As we conduct our new clinical programs, we will generate new data and gain new insights that will help inform our development strategy in pursuit of additional indications in the future.

Our Commercialization Strategy

We launched WAKIX into the narcolepsy market in November 2019 and are engaging with HCPs, patients and payors through the focused commercialization strategy outlined below to optimize adoption of WAKIX in the marketplace:

- ***HCP Awareness and Adoption***: To facilitate HCP awareness and adoption of WAKIX, we have deployed our dedicated, in-house, over 70-person sales team to educate a defined prescriber base of approximately 8,000 HCPs comprised of neurologists, pulmonologists, sleep specialists, psychiatrists and high-prescribing primary care physicians who specialize in or focus on sleep disorders. We believe these HCPs diagnose and treat approximately 90% of the narcolepsy patients in the United States. We began our commercial HCP outreach in August 2019 following FDA approval of WAKIX for the treatment of EDS in adult patients with narcolepsy and our efforts continue following the approval of the cataplexy indication in October 2020.

- ***Patient Awareness***: It is estimated that narcolepsy affects approximately 165,000 Americans with fewer than 50% diagnosed. Of those living with narcolepsy in the United States, it is estimated that fewer than 45,000 are on narcolepsy medications, which we believe indicates a significant unmet medical need. To drive patient awareness of WAKIX and its differentiated product profile, we have been communicating with the narcolepsy patient community and providing them with educational materials and information on WAKIX.

- ***Payor Coverage:*** Recognizing the importance of payor coverage, our field market access team has been engaging with national and regional payors over the past two plus years to educate them on the clinical data and value proposition of WAKIX. Through December 31, 2020, we have secured formulary access for approximately 80% of all insured lives (Commercial, Medicare and Medicaid) in the United States. Within these covered lives, we have observed favorable access to WAKIX subsequent to the expanded approval of WAKIX for the treatment of cataplexy in adult patients with narcolepsy in October 2020.

We believe the differentiating attributes of WAKIX that have facilitated and will continue to facilitate awareness, adoption, and coverage include: (i) it is a first-in-class molecule with a novel MOA, (ii) it is the first-and-only non-scheduled treatment approved for EDS or cataplexy in adult patients with narcolepsy, (iii) it is not a stimulant, (iv) it has broad clinical utility because it can be used as monotherapy or administered concomitantly with other narcolepsy treatments, and (v) it is a once-daily oral tablet administered in the morning upon wakening.

Clinical Development of WAKIX (pitolisant)

Overview

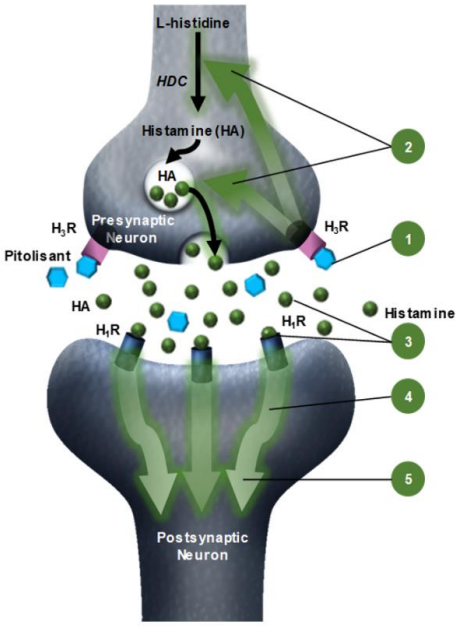
The strategy behind the clinical development of pitolisant is based on its MOA, which is thought to work by regulating histamine transmission. Pitolisant is a first-in-class molecule with a novel MOA, acting as a potent and highly selective antagonist/inverse agonist of the H_3 receptor. It activates histaminergic neurons in the brain, a neuronal system involved in the maintenance of wakefulness, attention, vigilance and cognition. Pitolisant binds to H_3 receptors on presynaptic neurons and blocks the normal negative feedback mechanism for histamine release, resulting in increased release of this wake-promoting neurotransmitter. It also functions as an inverse agonist, resulting in enhanced histamine synthesis and release from presynaptic neurons. Increased histamine available in the synapse binds to postsynaptic H_1 receptors, activating postsynaptic neurons, which stimulate wake-promoting brain regions and inhibit sleep-promoting regions of the brain.

WAKIX® (pitolisant) Mechanism of Action

Pitolisant is a histamine H_3-receptor antagonist/inverse agonist that enhances the activity of histaminergic neurons in the brain

1. Pitolisant blinds to presynaptic H_3 auto-receptors, which blocks histamine binding to these receptors and increases histamine release from presynaptic neurons
2. Acting as an inverse agonist, pitolisant initiates increased histamine synthesis and release from vesicles into the synapse
3. This increased histamine in the synapse is then available to bind to excitatory postsynaptic H_1 receptors
4. Increased histamine binding at H_1 receptors results in an increase in neuronal firing of postsynaptic neurons
5. Increased firing of histamine neurons further activates wake-associated brain regions and inhibits non-REM and REM sleep-associated brain regions

HA = Histamine; HDC = L-histidine decarboxylase
H_3R = Histamine 3 Receptor
H_1R = Histamine 1 Receptor



Receptor Figure adapted from: Benarroch EE. Neurology. 2010;75(16):1472-1479.

Pitolisant also stimulates the release of other wake-promoting neurotransmitters (dopamine, norepinephrine, serotonin and acetylcholine) via H_3 heteroreceptors within those neuronal systems. Importantly, pitolisant does not increase dopamine levels in the striatum, including the nucleus accumbens, which is the brain's reward center where an increase in dopamine levels is correlated with abuse potential. This feature of pitolisant's MOA, along with primarily working through the histaminergic system, are two of the aspects that differentiate pitolisant from all other currently approved treatments for narcolepsy.

The safety profile of pitolisant is based on pooled safety data from 22 Phase 2 or Phase 3 clinical trials conducted by Bioprojet, eight of which were in patients with narcolepsy and 14 of which were in other indications. These trials included 1,513 unique patients, of whom 1,043 received pitolisant in double-blind placebo-controlled studies, and others received pitolisant in single-blind or open-label trials. Three successful pivotal trials in narcolepsy, HARMONY 1, HARMONY 1bis, and HARMONY CTP, were completed in Europe by Bioprojet and served as the foundation for the approval of pitolisant by the EMA in 2016 for the treatment of narcolepsy in adults with or without cataplexy. Pitolisant was evaluated in a long-term safety and tolerability trial, HARMONY 3, which further supported the results observed in HARMONY 1, HARMONY 1bis, and HARMONY CTP. The data from these trials were submitted, along with data from a human abuse potential ("HAP") trial, to the FDA as part of the NDA for WAKIX (pitolisant), which the FDA approved on August 14, 2019 for the treatment of EDS in adult patients with narcolepsy and on October 13, 2020 for the treatment of cataplexy in adult patients with narcolepsy. The table below provides an overview of the trial designs from these five clinical trials.

Name of Study Study Design	Number of Patients	Maximum Dose; % at that Dose	Primary Objective	Results
HARMONY 1 Randomized, double-blind, placebo and active control; patients with narcolepsy ± cataplexy; 8 weeks of treatment	N = 95	35.6 mg; 61%	Assess change in Epworth Sleepiness Scale (“ESS”) score from baseline to final visit	-6.0 for WAKIX compared to -2.9 for placebo (treatment effect -3.1; p=0.022)
HARMONY 1bis Randomized, double-blind, placebo and active control; patients with narcolepsy ± cataplexy; 8 weeks of treatment	N = 166	17.8 mg 76%	Assess change in ESS score from baseline to final visit	-5.0 for WAKIX compared to -2.8 for placebo (treatment effect -2.2; p=0.030)
HARMONY CTP Randomized, double-blind, placebo control; patients with narcolepsy and cataplexy; 7 weeks of treatment	N = 106	35.6 mg 65%	Assess change in Weekly Rate of Cataplexy (“WRC”)	WRC decreased 75% for WAKIX compared to 38% for placebo (rate ratio 0.51; p<0.0001)
HARMONY 3 Long-term, open-label, real-world trial; ≥1 year	N = 104	35.6 mg 88%	Long-term safety	Safety/tolerability profile consistent with that seen in the RCTs
Human Abuse Potential Study Randomized, double-blind, active & placebo-controlled, 4-way crossover study	N = 43	35.6 mg & 213.6 mg; Phentermine 60 mg (active control)	Assess drug liking	WAKIX demonstrated a statistically significant and clinically relevant reduction in drug liking (p<0.0001)

Clinical Trial Highlights

The key findings from these clinical trials are as follows:

- Pitolisant showed a statistically significant improvement in EDS in adult patients with narcolepsy. In HARMONY 1, the ESS score change from baseline to final visit was -6.0 for pitolisant compared to -2.9 for placebo (treatment effect -3.1; p=0.022). In HARMONY 1bis, the ESS score change from baseline to final visit was -5.0 for pitolisant compared to -2.8 for placebo (treatment effect -2.2; p=0.030). These findings were supported by statistically significant improvement on the Maintenance of Wakefulness Test (“MWT”).

- Pitolisant demonstrated a statistically significant reduction in measures of cataplexy in adult patients with narcolepsy. In HARMONY CTP, the reduction in the weekly rate of cataplexy in patients on pitolisant was

75% compared to 38% in patients on placebo (rate ratio 0.51; 95% CI 0.44 – 0.60; p<0.0001). This finding was supported by a significant reduction in cataplexy (a secondary endpoint) in the HARMONY 1 trial. However, the FDA initially stated that the cataplexy data from the HARMONY 1 trial in the NDA did not provide substantial evidence of effectiveness with respect to cataplexy because the statistical analysis plan did not prospectively control for Type 1 error of the secondary endpoints, and the subgroup of patients with cataplexy was not identified prospectively. As a result, the FDA issued a complete response letter ("CRL") with respect to the cataplexy indication, and therefore did not originally approve WAKIX for the treatment of cataplexy in adult patients with narcolepsy. Subsequently, in June 2020, in response to our request for FDA to reconsider the cataplexy data from the HARMONY 1 trial, we received a general advice letter confirming that the cataplexy data from the HARMONY 1 clinical trial supported a statistically significant reduction in daily rate of cataplexy in the pitolisant group when compared with the placebo group. As a result, the FDA recommended we submit a complete response resubmission in pursuit of the adult cataplexy indication for WAKIX. On October 13, 2020, we received regulatory approval for WAKIX for the treatment of cataplexy in adult patients with narcolepsy.

- Pitolisant was generally well-tolerated in clinical trials. In the placebo-controlled clinical trials conducted in patients with narcolepsy with or without cataplexy, the most common adverse reactions (occurring in ≥5% of patients and at twice the rate of placebo) with the use of pitolisant were insomnia (6%), nausea (6%), and anxiety (5%). In these trials, 6 of the 152 patients (3.9%) who received pitolisant and 4 of the 114 patients (3.5%) who received placebo discontinued because of an adverse event.

- In the HARMONY 3 trial, a favorable long-term safety/tolerability profile for pitolisant out to one year was demonstrated; safety findings were similar to those reported in the randomized controlled trials, with no new safety signals identified.

    - In this open-label, long-term real-world trial, improvement in EDS (as measured by a reduction in ESS scores) and reduction in cataplexy (as measured by reduction in mean daily cataplexy episodes) was maintained out to twelve months.

- In a clinical HAP trial, pitolisant demonstrated statistically significant lower maximum drug liking (primary endpoint), overall drug liking, and willingness to take drug again compared to phentermine (C-IV), with responses similar to placebo. No evidence of abuse potential was demonstrated based on clinical and preclinical data, and WAKIX was therefore approved without being scheduled as a controlled substance by the DEA.

HARMONY 1

Design

HARMONY 1 was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of pitolisant in adult patients with narcolepsy on improvement in EDS over an eight-week period. The trial was conducted in the EU, and consequently was designed to include both a placebo arm and an active comparator, modafinil, which was used in doses up to 400 mg/day. HARMONY 1 consisted of 95 patients and had flexible dosing during the first three weeks of the trial, followed by five weeks of stable dosing. The maximum dose of pitolisant in this dose-to-effect trial was 35.6 mg and only 61% of the patients were titrated to this dose for the stable dosing period. Approximately 80% of the patients had a history of cataplexy.

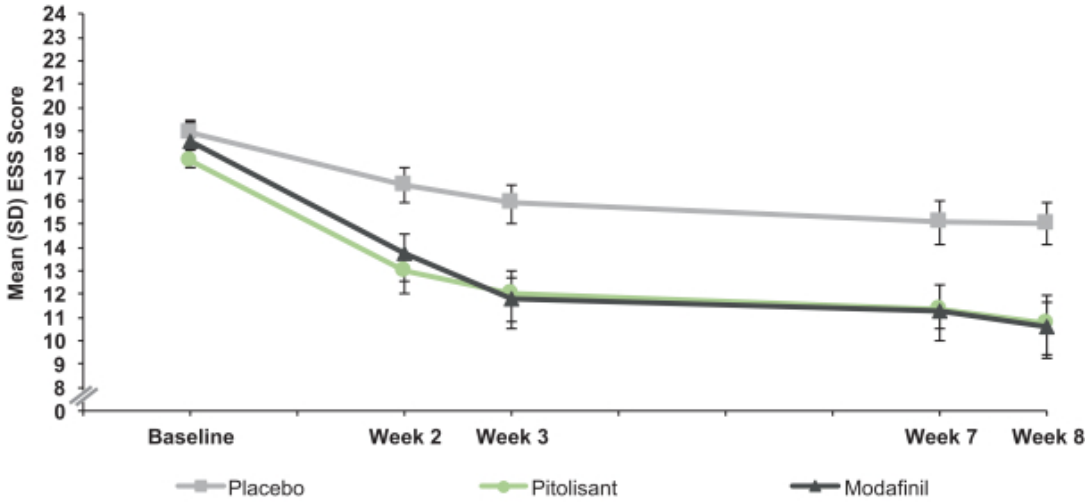
The primary endpoint in the trial was the ESS score at final visit, adjusted for baseline, for pitolisant compared to placebo. ESS is a self-administered eight-item questionnaire scored 0 to 24 with lower scores corresponding to lower EDS. Secondary endpoints in HARMONY 1 included ESS responder rates, MWT (an objective measure of the ability to stay awake), the Sustained Attention to Response Task ("SART") reduction in cataplexy, Clinical Global Impression of Change ("CGI-C") for both EDS and cataplexy, the European Quality of Life Questionnaire (the "EQ-5D"), and the Patient's Global Opinion on the Effect of Treatment Questionnaire. The main efficacy objective of the trial was to demonstrate superiority of pitolisant compared to placebo on the primary

endpoint, while one of the secondary objectives was to explore the non-inferiority of pitolisant compared to modafinil on ESS score. It should be noted that there was no prospective plan to control for Type 1 error in this trial.

Efficacy Results

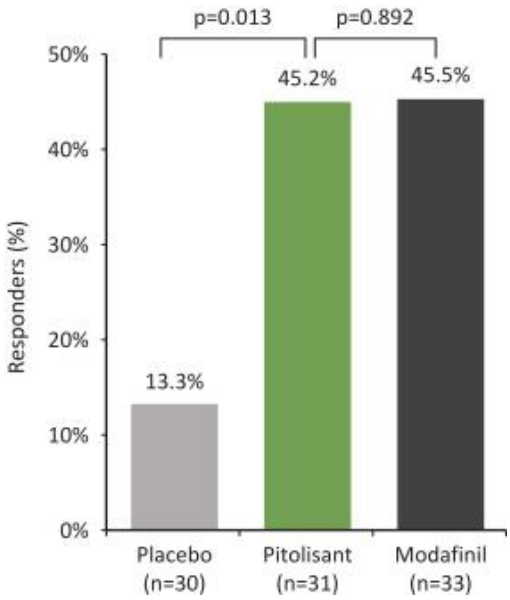
Pitolisant showed a significant reduction in the mean ESS score change from baseline to final visit at end of trial as compared to placebo (-6.0 versus -2.9, respectively) and between-group differences in ESS score were evident within the first two weeks of treatment. This resulted in a treatment effect (ESS score at final visit, adjusted for baseline, for pitolisant compared to placebo) of -3.1, which was statistically significant for pitolisant versus placebo (p=0.022). The change from baseline in ESS score for modafinil was -6.9 and, based on this score, pitolisant was not found to be non-inferior to modafinil (mean difference of 0.09, p=0.932) and the trial therefore did not meet this secondary efficacy objective. We believe there are several factors that contributed to this finding. First, 73% of the patients on modafinil in this trial were titrated up to a dose of 400 mg/day (the recommended dose of modafinil in the FDA-approved U.S. Prescribing Information ("USPI") is 200 mg/day) while only 61% of the patients on pitolisant were titrated to the maximum pitolisant dose of 35.6 mg/day (which is the maximum approved dose in the USPI), such that a greater number of patients in the modafinil arm received the maximum effective dose than those in the pitolisant arm, raising the possibility that those subjects in the pitolisant arm could have seen greater treatment effect had they been dosed at the maximum dose available. Second, the margin of non-inferiority for the difference in the ESS scores pre-specified in the statistical analysis plan was narrow (2 points), meaning that the change in ESS score adjusted for baseline compared between pitolisant and modafinil had to have a lower 95% CI of no less than -2 points to declare pitolisant non-inferior to modafinil. The lower bound of the 95% CI of the analysis fell just outside this margin (-2.11). According to literature, however, a clinically relevant difference on the ESS ranges from 2–3 points, such that the non-inferiority margins pre-specified under the statistical analysis plan may have been too narrow. Ultimately, however, the trial results comparing pitolisant and modafinil did not impact the FDA's findings that pitolisant was effective for improvement in EDS, and the FDA-approved label for WAKIX does not contain any data on modafinil.

Change in ESS Score Over Time

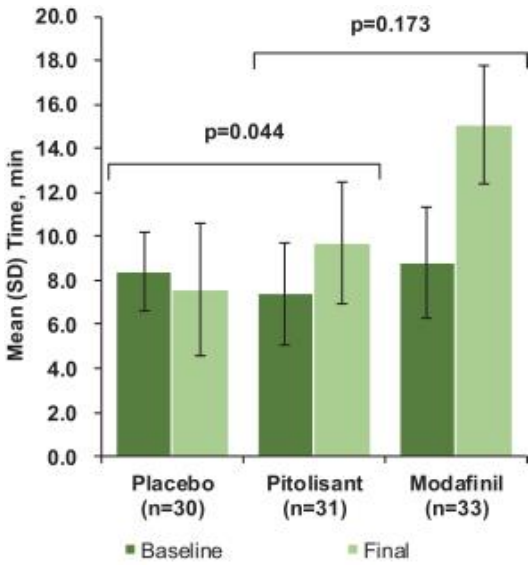


Regarding the secondary endpoints, ESS responder rates (a responder was defined as having a final ESS score $\leq$ 10) were significantly greater for those patients treated with pitolisant compared to those on placebo (45.2% vs. 13.3%, respectively; p=0.013). The responder rate for patients treated with modafinil was 45.5% and the difference compared to pitolisant was not statistically significant (p=0.892). On the MWT, pitolisant treatment improved performance when compared to placebo in a statistically significant manner (p=0.044), while improvement was not significantly different compared to modafinil (p=0.173).

Responders (Final ESS ≤ 10)



Change in MWT



With regard to other secondary endpoints, the overall pattern of response was that the findings for patients on both pitolisant and modafinil were superior to those on placebo while the responses were not significantly different for pitolisant compared to modafinil. The SART Total Score (a measure of attention) was significantly higher in the pitolisant group as compared to placebo (p=0.041), and while not significantly different from the modafinil group (p=0.363), the scores were similar (9.1 and 8.9 for pitolisant and modafinil, respectively). The CGI-C for EDS showed improvement in 56% of patients on placebo, 73% of patients on pitolisant, and 86% of patients on modafinil. Regarding the daily cataplexy rates endpoint, patients treated with pitolisant experienced a 62% reduction in the daily rate of cataplexy compared to a reduction of 8% in those on placebo and 25% in those on modafinil. Responses on the CGI-C for cataplexy were consistent with this outcome, with 29%, 45%, and 35% of patients who experienced cataplexy during the trial reporting an improvement in their cataplexy symptoms in the placebo, pitolisant, and modafinil groups, respectively. Lastly, the Patient's Global Opinion on the Effect of Treatment Questionnaire recorded positive responses in 56% of patients in the placebo group, 81% of patients in the pitolisant group, and 86% of patients in the modafinil group.

Safety Results

Pitolisant was generally well tolerated in HARMONY 1. Sixty patients experienced a treatment emergent adverse event ("TEAE") during the trial: 61% in the pitolisant group, 60% in the placebo group, and 70% in the modafinil group. The most commonly reported TEAE in the pitolisant treatment group was headache, reported by 35% of the patients, compared to 20% in the placebo group. Other frequently reported TEAEs in the pitolisant treatment group were insomnia, nausea and weight increase (each reported by two patients, or 6%). There were five serious adverse events during HARMONY 1 and none were considered treatment-related (two in the pitolisant group, two in the modafinil group, and one in the placebo group). There were no deaths during the trial and no significant changes in laboratory values or hemodynamic parameters (heart rate and blood pressure) from baseline to final visit in any group.

HARMONY 1bis

HARMONY 1bis was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of pitolisant in adult patients with narcolepsy on improvement in EDS over an eight-week period. This trial

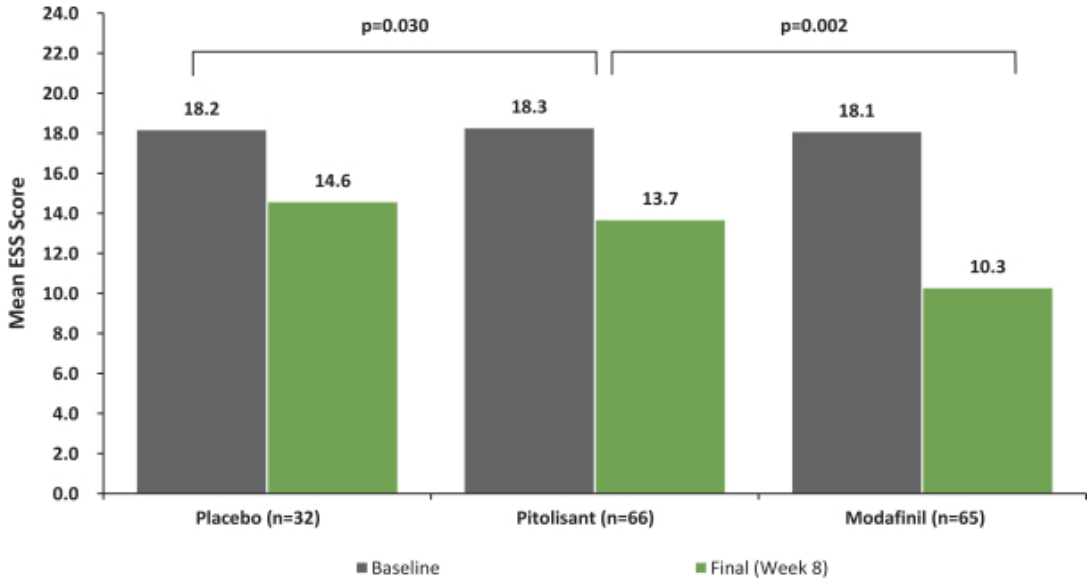
was designed in accordance with recommendations from European regulators, and as such, contained both a placebo and active comparator arm. The active comparator was modafinil used in doses up to 400 mg/day. HARMONY 1bis enrolled 165 patients and had flexible dosing during the first three weeks of the trial, followed by five weeks of stable dosing. The maximum dose of pitolisant in this dose-to-effect trial was 17.8 mg and only 76% of the patients were titrated to this dose for the stable dosing period. 75% of the patients had a history of cataplexy.

The primary endpoint in the trial was the ESS score at final visit, adjusted for baseline, for pitolisant compared to placebo. Secondary endpoints included ESS responder rates, MWT, SART, reduction in cataplexy, CGI-C for both EDS and cataplexy, the EQ-5D, and the Patient's Global Opinion on the Effect of Treatment Questionnaire. The main efficacy objective of the trial was to demonstrate superiority of pitolisant compared to placebo on the primary endpoint, while one of the secondary objectives was to explore the non-inferiority of pitolisant compared to modafinil on ESS score. It should be noted that there was no prospective plan to control for Type 1 error in this trial.

Efficacy Results

Pitolisant showed a significant reduction in the mean ESS score change from baseline to final visit as compared to placebo (-5.0 versus -2.8, respectively). This resulted in a treatment effect (ESS score at final visit, adjusted for baseline, for pitolisant compared to placebo) of -2.2 (p=0.030). The treatment effect between modafinil and pitolisant was -2.75 and, based on this score and the pre-specified statistical analysis plan, resulted in pitolisant not being non-inferior to modafinil. We believe the same factors that contributed to this result in HARMONY 1 also apply to HARMONY 1bis. In addition, in this trial, the maximum dose of pitolisant to which patients could be titrated (17.8 mg) was not the maximum labeled dose for pitolisant (which is 35.6 mg), and 24% of patients in this trial were on doses lower than 17.8 mg, which means that a substantial percentage of patients were on study drug at an amount less than the maximum approved dose in the USPI for pitolisant. In addition, modafinil was dosed up to 400 mg/day, while the recommended dose of modafinil in its USPI is 200 mg/day, which means that the respective doses of pitolisant and modafinil were not comparable.

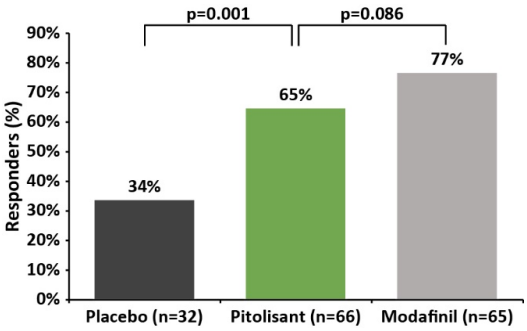
Change in Mean ESS Score



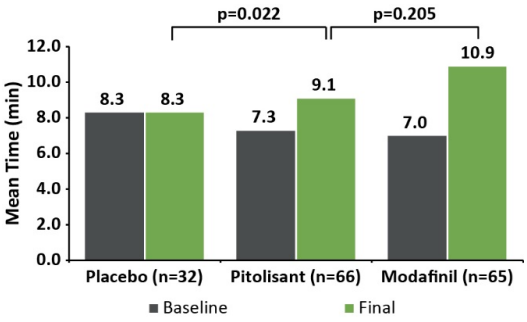
Regarding the secondary endpoints, ESS responder rates (a responder was defined as having a final ESS score $\leq$ 10 or change in ESS score $\geq$ 3) were significantly greater for those patients treated with pitolisant compared to those on placebo (65% vs. 34%, respectively; p=0.001). The responder rate for patients treated with modafinil

was 77% and the difference compared to pitolisant was not statistically significant (p=0.086). On the MWT, pitolisant treatment significantly improved performance when compared to placebo (p=0.022), while improvement was not significantly different compared to modafinil (p=0.294).

Responders (Final ESS ≤ 10 or Change in ESS ≥ 3)



Change in MWT



With regard to other secondary endpoints, the overall pattern of response was that the findings for patients on both pitolisant and modafinil were superior to those on placebo while the responses were not significantly different for pitolisant and modafinil. The pitolisant group's SART Total Score was significantly improved compared to placebo (p=0.043), while not significantly different compared to modafinil (p=0.407). The CGI-C for EDS showed improvement in 37% of patients on placebo, 72% of patients on pitolisant, and 78% of patients on modafinil. Responses on the CGI-C for cataplexy showed improvement for 60% of patients treated with pitolisant compared to 54% of patients on modafinil and 36% of patients on placebo. However, the difference in the reduction in the daily rate of cataplexy between pitolisant (0.32) and placebo (0.31) was not statistically significant (p=0.873). Lastly, the findings on both the EQ-5D and the Patient's Global Opinion on the Effect of Treatment Questionnaire did not show any meaningful differences between the pitolisant and placebo treatment groups in the HARMONY 1bis trial.

Safety Results

Pitolisant was generally well tolerated in HARMONY 1bis. Seventy-seven patients experienced a TEAE during the trial: 49% in the pitolisant group, 36% in the placebo group, and 49% in the modafinil group. The most commonly reported TEAEs in the pitolisant treatment group were headache (13%), dizziness (6%), vomiting (4.5%), insomnia (4.5%), and decreased appetite (4.5%). There were no serious adverse events in the pitolisant group and there was one serious adverse event during HARMONY 1bis in the modafinil treatment group, which was not treatment-related. There were no deaths during the trial and no significant changes in laboratory values or hemodynamic parameters (heart rate and blood pressure) from baseline to final visit.

HARMONY CTP

Design

HARMONY CTP was a randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of pitolisant on the reduction in cataplexy in adult patients with narcolepsy with frequent attacks of cataplexy over a seven-week period. HARMONY CTP consisted of 106 patients. The maximum dose of pitolisant in this dose-to-effect trial was 35.6 mg and only 65% of patients reached this dose during the stable dosing period. Both stimulants and wake-promoting agents were prohibited during the trial; only 11% of subjects were on stable doses of anti-cataplectic medications (7% in the pitolisant treatment group and 16% in patients on placebo).

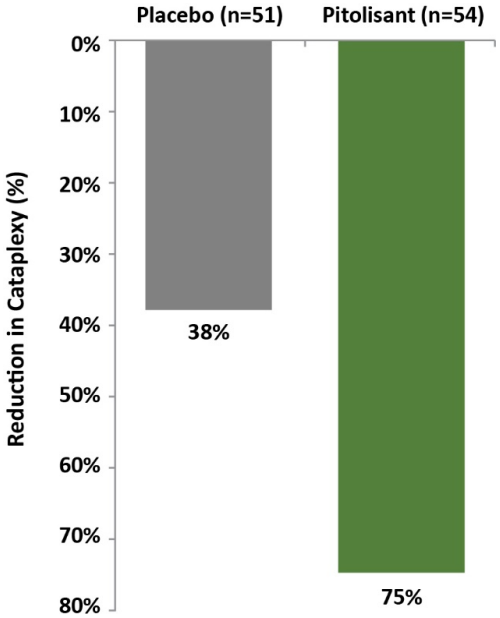
The primary endpoint in HARMONY CTP was the change in the weekly rate of cataplexy ("WRC") from baseline to the stable dosing period (Weeks 4–7) expressed as the rate ratio (change in the pitolisant group/change in the placebo group). Secondary endpoints included proportion of patients with high cataplexy rate (WRC >15), CGI-

C for cataplexy and EDS, mean change in ESS score and percentage of ESS responders, MWT, the EQ-5D, number of days with hallucinations (as recorded in the patient diaries), and Patient's Global Opinion on the Effect of Treatment Questionnaire. It should be noted that there was no prospective plan to control for Type 1 error in this trial.

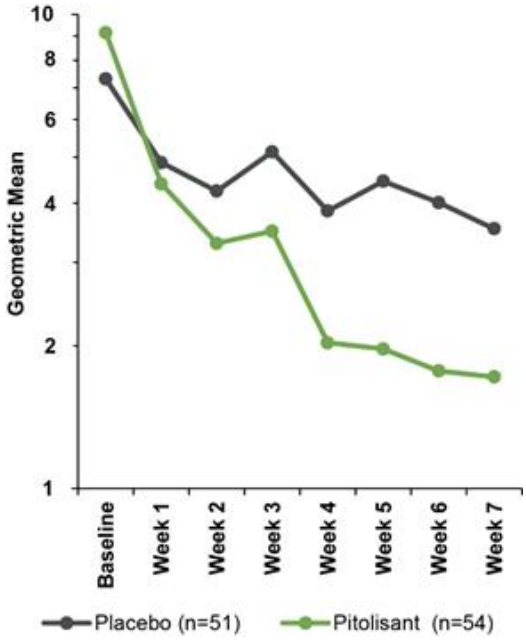
Efficacy Results

In HARMONY CTP, pitolisant resulted in a significantly greater reduction than placebo in the WRC from baseline to the stable dosing period (Weeks 4–7), with a 75% reduction in the pitolisant group compared to a 38% reduction in the placebo group (rate ratio 0.51; 95% CI (0.44, 0.60; p<0.0001). Further, significantly fewer patients had WRC >15 at endpoint with pitolisant (6%) versus placebo (24%) (p=0.005). The clinical relevance of these findings was captured by the CGI-C related to cataplexy. Mean CGI-C score was 3.5±1.1 with placebo versus 2.6±1.1 with pitolisant. The mean reduction of the CGI-C score for pitolisant compared with placebo was -0.95 (95% CI (-1.36, -0.54); p<0.0001). Overall positive response rates on the CGI-C related to cataplexy were 67% on pitolisant and 33% on placebo.

Percent Reduction in WRC

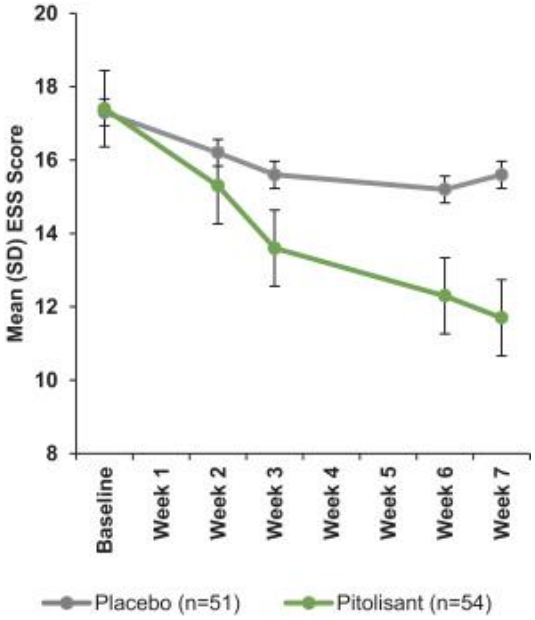


Reduction in WRC Over Time

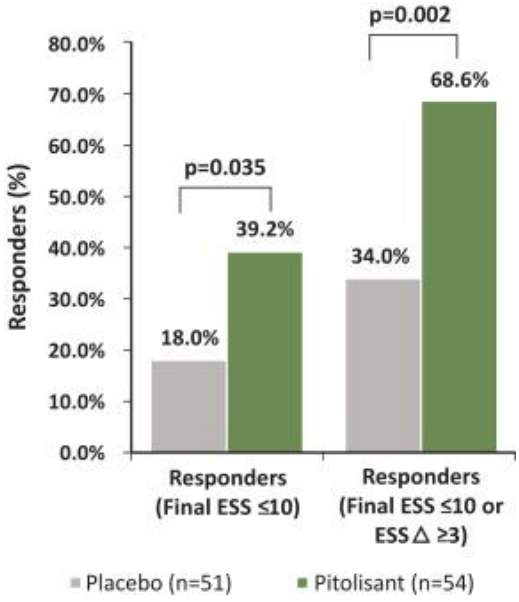


With regard to other secondary endpoints, pitolisant demonstrated a statistically significant reduction in mean ESS score from baseline to final visit at week seven as compared to placebo (-5.4 vs. -1.9; p=0.0001) and significantly higher ESS responder rates compared to placebo (p=0.035 for Type 1 ESS responders rate and p=0.002 for Type 2 ESS responders rate; see graph below). On the CGI-C related to EDS, the mean score was 3.7 with placebo versus 2.6 with pitolisant, with a mean reduction of -0.99 (p<0.0001). Overall positive response rates on the CGI-C related to EDS were 69% on pitolisant and 24% on placebo.

Change in ESS Score Over Time



ESS Responder Rate



On the remainder of the secondary endpoints, pitolisant showed a statistically significant improvement on the MWT from baseline to end of trial compared to placebo. Baseline geometric means on the MWT were 4.3 minutes and 3.7 minutes for placebo and pitolisant, respectively, with final MWT values of 4.6 minutes and 7.1 minutes for placebo and pitolisant, respectively; the improvement in MWT was 78% higher with pitolisant compared to placebo (p=0.003). On the Patient's Global Opinion on the Effect of Treatment Questionnaire, overall improvement was reported in 54% of patients on pitolisant and 26% of patients on placebo (p=0.001).

Safety Results

Pitolisant was generally well tolerated in HARMONY CTP. Thirty-five patients experienced a TEAE during the trial: 35% in the pitolisant group and 31% in the placebo group. The most commonly reported AE in the pitolisant group in HARMONY CTP was headache, which 9% of the group reported, compared to 10% in the placebo group. Other frequently reported AEs in the pitolisant group were irritability, anxiety and nausea (each reported by 3 patients, or 6%). There were no deaths or serious adverse events during HARMONY CTP and no significant changes in laboratory values or hemodynamic parameters (heart rate and blood pressure) from baseline to final trial visit in either group.

HARMONY 3

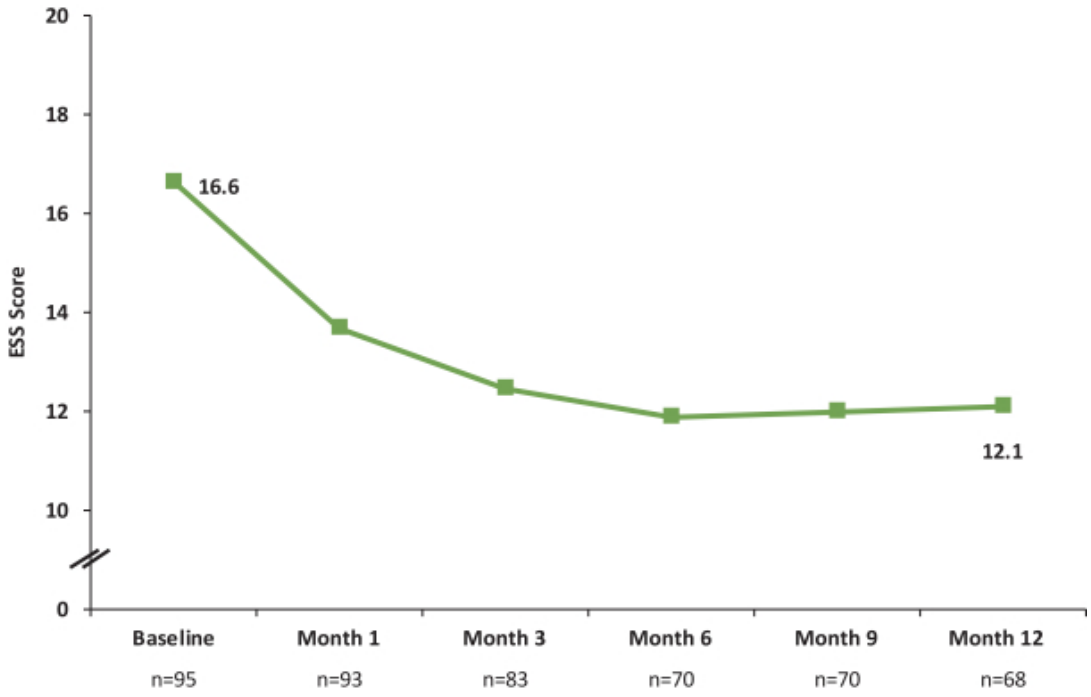
Design

HARMONY 3 was an open-label, real-world trial to assess the long-term safety and tolerability of pitolisant in the treatment of EDS in adult patients with narcolepsy, with or without cataplexy, over a one-year period (with a 5-year extension at the trial sites in France). HARMONY 3 enrolled 104 patients, 102 of whom were treated with pitolisant, and 68 completed out to one year. In HARMONY 3, 75% of patients had a history of cataplexy and 76% of patients who completed out to one year were on the maximum dose of pitolisant of 35.6 mg. For the 5-year extension phase at the trial sites in France, 50 patients were eligible to continue, of which 48 patients elected to do so and 32 of them were maintained on pitolisant out to 5 years or until the study ended.

Efficacy Results

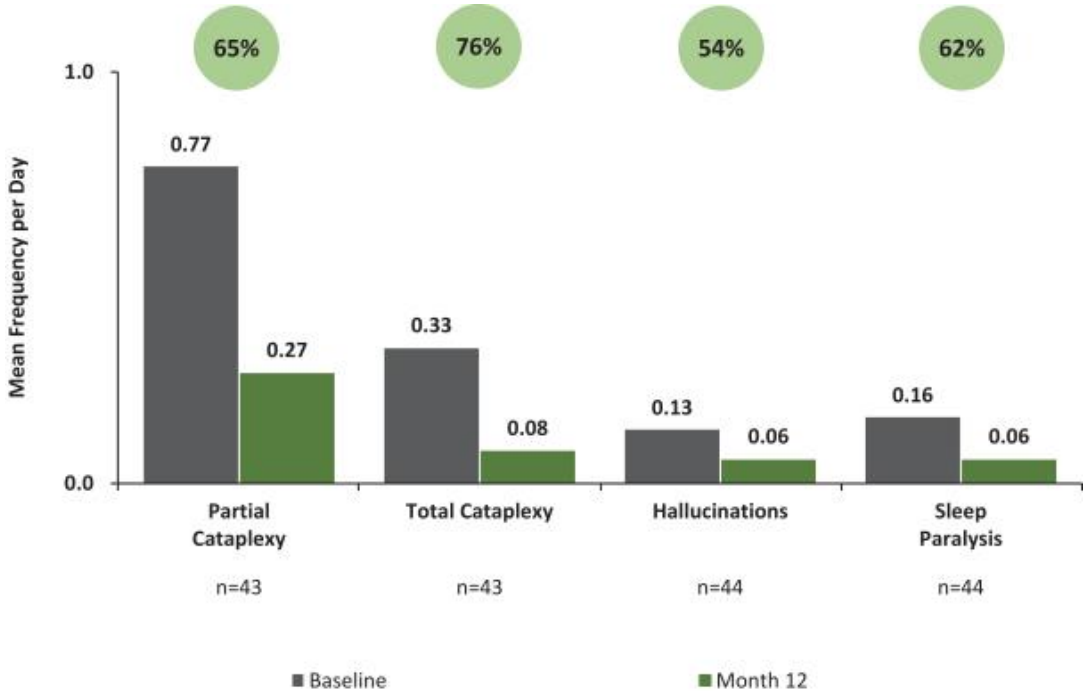
In the 68 patients with data at baseline and at 12 months in HARMONY 3, pitolisant reduced the mean ESS score by -4.63 over this period. The magnitude of the decrease in ESS score was larger in the subgroup of patients (n=86) who were not on pitolisant at trial entry (-5.25) as compared to the subgroup of patients (n=16) who came into the trial on pitolisant from the French Compassionate Use Program (-2.63).

ESS Score Over Time



In HARMONY 3, pitolisant also demonstrated a reduction in cataplexy and other symptoms of REM intrusion into wakefulness from baseline to month 12, showing a reduction of 65% to 76% in partial or total cataplexy attacks, respectively, out to one year. Reductions of more than 50% were also seen for other symptoms of REM dysfunction, such as hallucinations and sleep paralysis.

Reduction in Cataplexy and Other Symptoms of REM Dysfunction with Pitolisant



Safety Results

Pitolisant was generally well tolerated in HARMONY 3. AEs observed with long-term pitolisant treatment were consistent with those observed in short-term randomized, controlled trials such as HARMONY 1, HARMONY 1bis, and HARMONY CTP. Fifty-eight of the 102 treated patients (57%) reported an aggregate of 168 TEAEs in HARMONY 3, the most common of which are shown in the table below. During the one-year trial, there were no deaths and seven patients reported 10 serious adverse events, nine of which were deemed by the investigator to be unrelated to pitolisant, and one miscarriage which was considered possibly related. No clinically significant changes in laboratory parameters, vital signs or electrocardiogram parameters were recorded over the course of the one year trial.

Adverse Events (Incidence ≥ 3%), n (%)	**Total Population (N=102)**
Any adverse event	58 (56.9)
Headache	12 (11.8)
Insomnia	9 (8.8)
Weight increased	8 (7.8)
Anxiety	7 (6.9)
Depression	5 (4.9)
Nausea	5 (4.9)
Irritability	4 (3.9)
Vomiting	4 (3.9)
Vertigo	4 (3.9)

Clinical HAP Trial

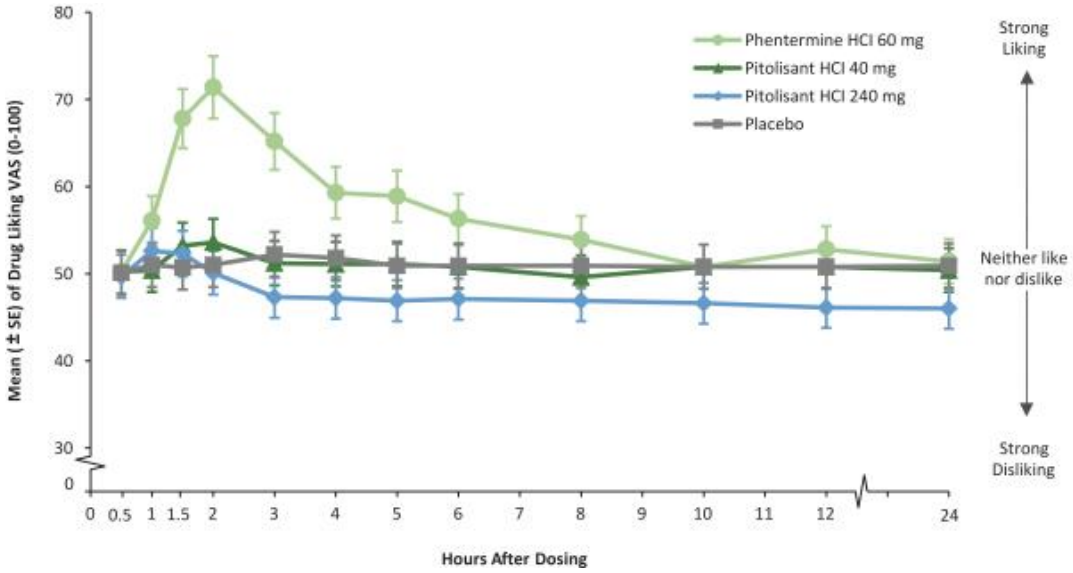
Design

A clinical HAP trial was conducted to evaluate the human abuse potential of pitolisant. In this trial, nondependent, recreational stimulant users able to distinguish phentermine hydrochloride (HCl; 60 mg), a CIV stimulant, from placebo in a drug discrimination test were randomized in a 4-period, double-blind, crossover design to receive single doses of pitolisant 35.6 mg (therapeutic dose), pitolisant 213.6 mg (supra-therapeutic dose), phentermine HCl 60 mg, and placebo. The primary endpoint was maximum effect (Emax) on the 100-point Drug Liking (at the moment) visual analog scale.

Results

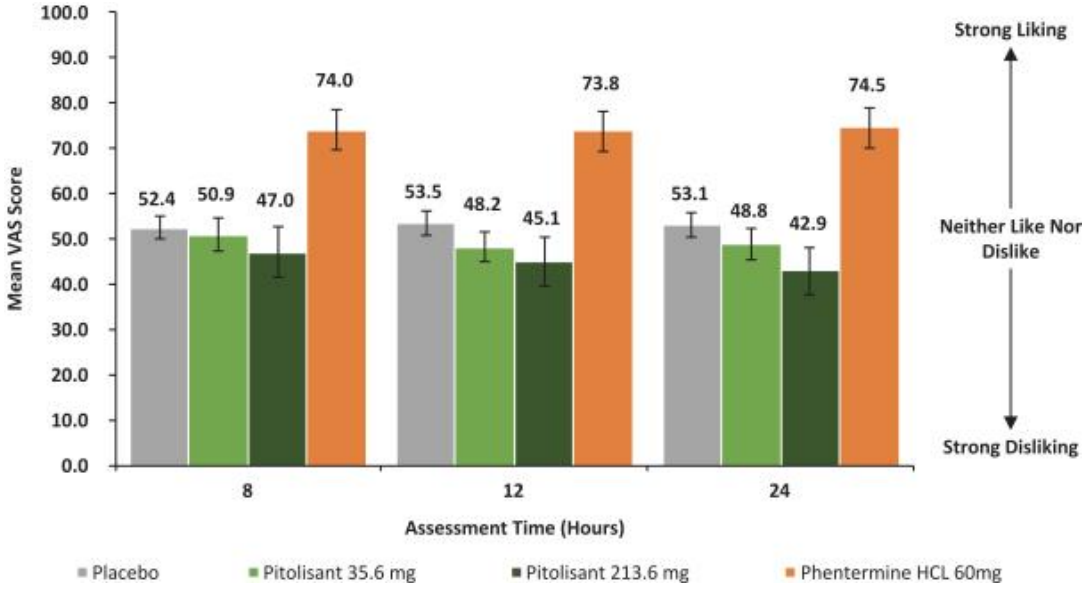
A total of 43 subjects were enrolled and 38 completed the trial. Mean Drug Liking Emax was significantly greater for phentermine (78.7) versus pitolisant 35.6 mg (57.3; p<0.0001) and pitolisant 213.6 mg (59.0; p<0.0001). Drug Liking Emax was similar for pitolisant (both doses) and placebo (56.1) (p<0.001 for 35.6 mg versus placebo, and p=0.003 for 213.6 mg versus placebo).

Maximum Drug Liking

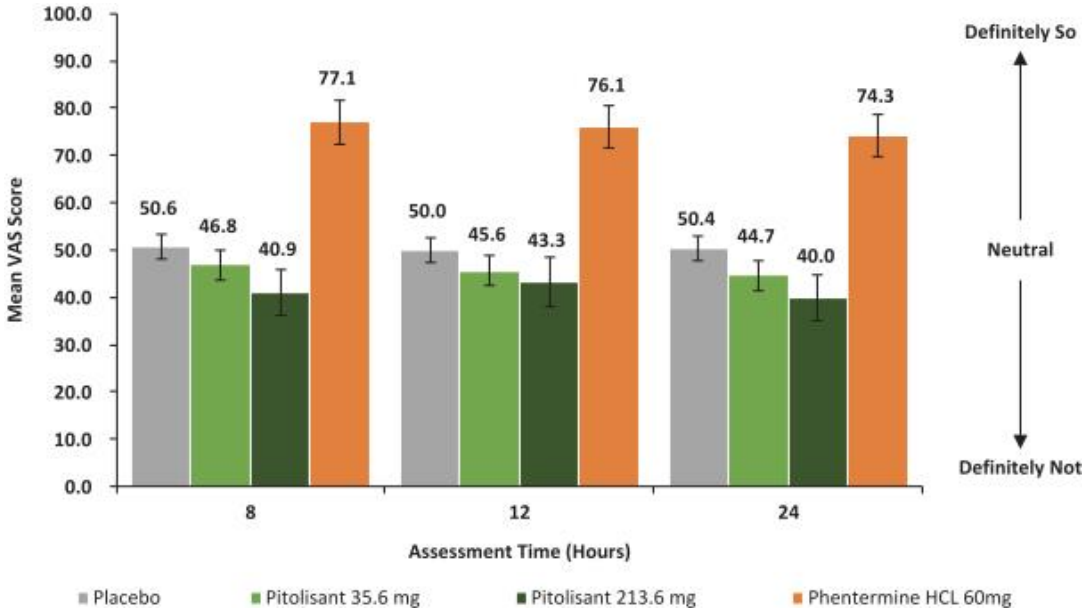


Similarly, for key secondary measures of Overall Drug Liking and willingness to Take Drug Again, mean Emax scores were significantly greater for phentermine (77.4 for Overall Drug Liking and 78.7 for Take Drug Again) versus pitolisant 213.6 mg (49.3 and 44.5) and 35.6 mg (52.7 and 49.4) ($p <$ 0.0001 for each comparison for both doses of pitolisant compared to phentermine).

Overall Drug Liking



Take Drug Again

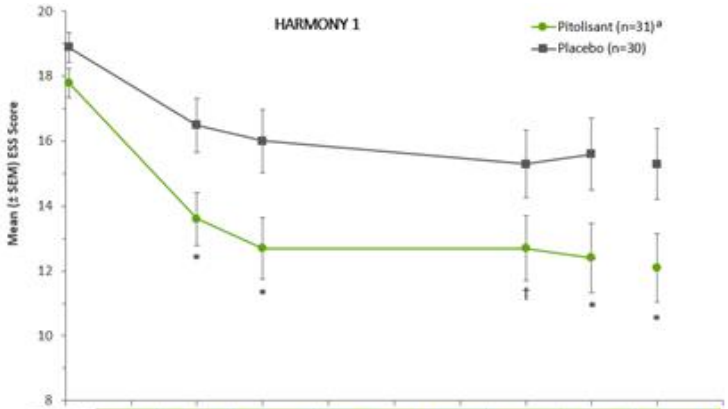


In summary, in the clinical HAP trial, pitolisant demonstrated a statistically significant and clinically relevant reduction in drug liking compared to phentermine as well as an overall response profile similar to placebo. Based on these clinical data, along with data from preclinical abuse liability studies, the evidence pointed to a low risk of abuse for pitolisant, which supported the approval of WAKIX without being scheduled as a controlled substance by the DEA.

Post-Hoc Analyses for Pitolisant

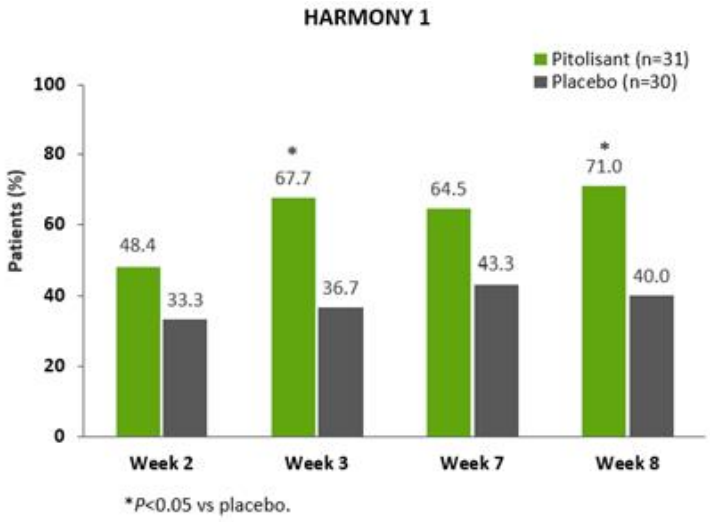
We conducted three post-hoc analyses from the database of the narcolepsy clinical trials for pitolisant, which focused on clinically relevant aspects of the product profile. The first analysis examined the time-to-onset of clinical response for pitolisant for improvement in both EDS and reduction in cataplexy based on data from 61 patients in the HARMONY 1 (pitolisant, n=31; placebo, n=30) and 105 patients in the HARMONY CTP (pitolisant, n=54; placebo, n=51) randomized, controlled clinical trials. Study medication was individually titrated to a potential maximum dose of pitolisant 35.6 mg/d and then remained stable; 61% of patients in HARMONY 1 and 65% in HARMONY CTP were titrated to the 35.6 mg dose. Efficacy assessments included the ESS and WRC or daily rate of cataplexy. Onset of clinical response was defined as the first timepoint at which there was a statistically significant difference between pitolisant and placebo. For time-to-response for EDS using the ESS, least-squares ("LS") mean change from baseline was significantly greater for pitolisant compared with placebo beginning at Week 2 in HARMONY 1 and Week 3 in HARMONY CTP (when patients were first able to receive the 17.8 mg dose in each study) and continued through the end of treatment. More pitolisant-treated patients were classified as treatment responders (ESS reduction of ≥ 3 points) at each post-baseline assessment than were patients in the placebo group. Pitolisant treatment resulted in a significantly greater proportion of responders versus placebo beginning at Week 3 in both studies. In HARMONY CTP, the frequency of cataplexy attacks was significantly reduced for pitolisant compared with placebo beginning at Week 2 and continued through the end of treatment. The percentage of cataplexy responders in HARMONY CTP was significantly greater with pitolisant versus placebo beginning at Week 1 for response defined as ≥ 25% reduction in WRC and at Week 2 for response defined as ≥ 50% reduction in WRC. There was no evidence of rebound cataplexy after a one-week placebo washout phase. In summary, the onset of clinical response was observed beginning at Week 2 (HARMONY 1) or Week 3 (HARMONY CTP) for mean change in ESS score and at Week 2 (HARMONY CTP) for mean change in WRC, with further improvements observed in pitolisant-treated patients through the end of treatment. The percentage of treatment responders was significantly greater with pitolisant versus placebo beginning at Week 3 for EDS (defined as ESS score reduction ≥ 3) and at Week 2 for cataplexy (defined as ≥ 50% reduction in WRC).

Time-to-Onset of Response for EDS Based on ESS Scores in HARMONY 1

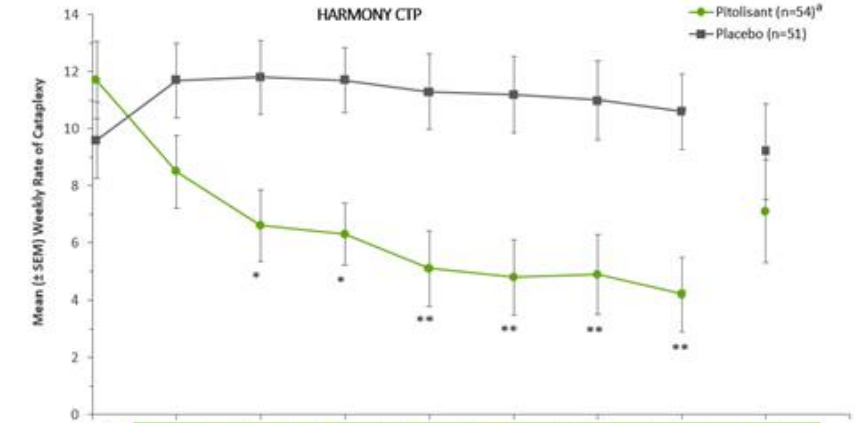


[a]Placebo washout phase: HARMONY 1: pitolisant, n=26; placebo, n=25.
*p<0.05 vs placebo; †p=0.05 vs placebo.

Time-to-Onset of Response for EDS Based on ESS Responder Rate (ESS reduction of ≥3 points) in HARMONY 1

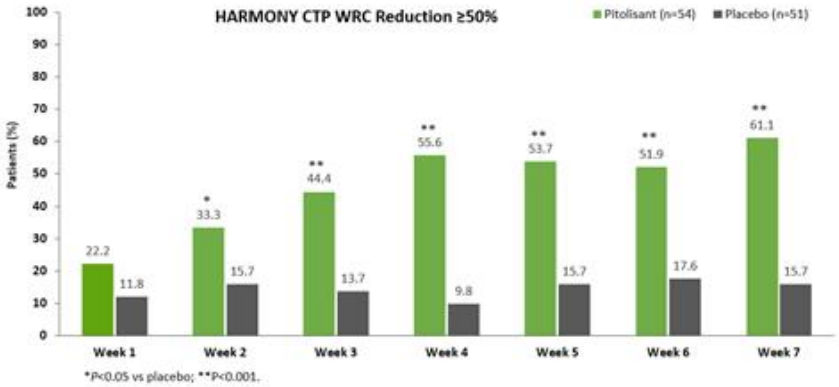


Time-to-Onset of Response for Cataplexy Based on WRC in HARMONY CTP



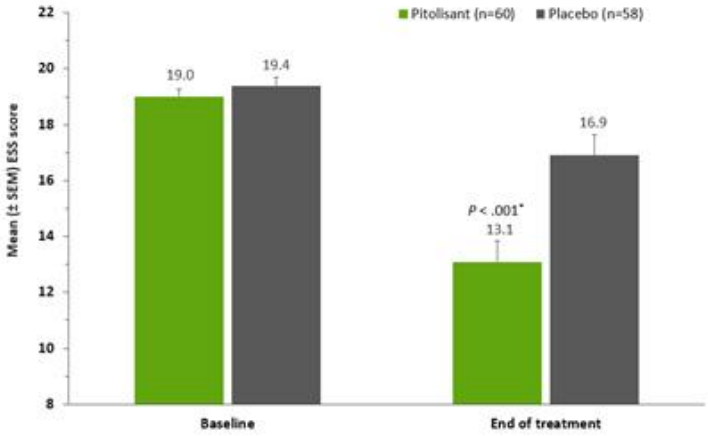
[a]Placebo washout phase, pitolisant, n=36; placebo, n=41.
*p<0.01 vs placebo; **p<0.001 vs placebo.

Time-to-Onset of Response for Cataplexy Based on WRC Reduction ≥ 50% in HARMONY CTP

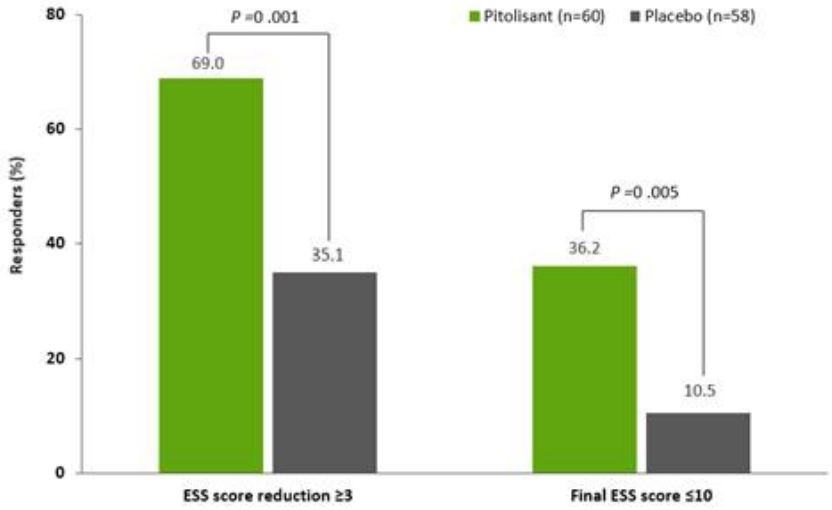


A second post-hoc analysis evaluated the efficacy of pitolisant in patients with narcolepsy who had a high symptom burden (both EDS and cataplexy) at baseline; this analysis was based on pooled data from both the HARMONY 1 and HARMONY CTP clinical trials, in which patients could be titrated up to a maximum dose of 35.6 mg/day. The analyses included three independent patient subgroups: baseline score of ≥16 on the ESS, sleep latency of ≤8 minutes on MWT, and ≥15 cataplexy attacks per week. The analysis populations included 118 patients for the ESS (pitolisant, n=60; placebo, n=58), 105 for the MWT (pitolisant, n=59; placebo, n=46), and 31 for cataplexy (pitolisant, n=20; placebo, n=11). LS mean change in ESS from baseline was significantly greater for pitolisant (-6.1) compared with placebo (-2.3; p<0.001). A significantly greater percentage of pitolisant-treated patients were classified as treatment responders: for ESS score reduction ≥3, 69.0% in the pitolisant group versus 35.1% in the placebo group (p=0.001); for final ESS score ≤10, 36.2% versus 10.5%, respectively (p=0.005). Mean increase in sleep latency on the MWT was significantly greater for pitolisant (6.9 minutes) compared with placebo (3.4 minutes; p=0.017). In patients with a high burden of cataplexy, LS mean change in the WRC was significantly greater for pitolisant (–14.5) compared with placebo (–0.1; P = 0.004). On average, the frequency of cataplexy attacks was reduced by 60.6% in the pitolisant group and <1% in the placebo group. Adverse events in the analysis populations were consistent with the known safety profile of pitolisant; headache was the most common adverse event in pitolisant-treated patients (10.0%–20.0%). These analyses demonstrated pitolisant resulted in significant improvement in patients who experience a high burden of the two most common symptoms in narcolepsy, EDS and cataplexy.

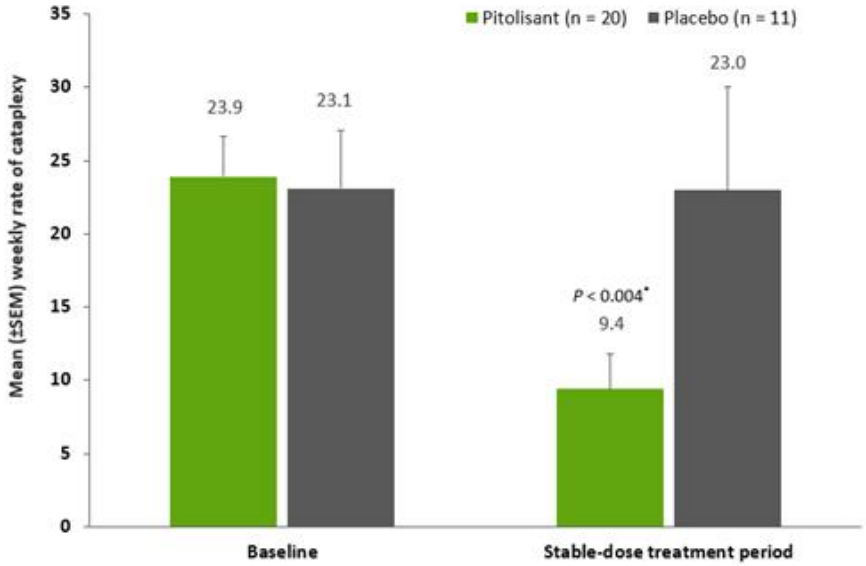
High Burden of EDS: Reduction in ESS Scores



High Burden of EDS: Treatment Responders Based on ESS Scores



High Burden of Cataplexy: Reduction in WRC



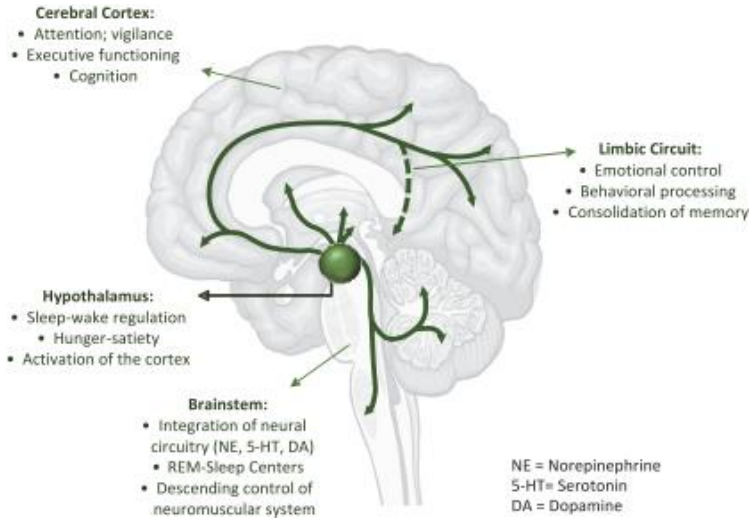
In the third post-hoc analysis, we evaluated the cardiac safety events associated with pitolisant because cardiovascular diseases are comorbid conditions in patients with narcolepsy. Cardiovascular adverse effects are of concern with narcolepsy medications because of this comorbidity and most patients require lifelong pharmacotherapy for both narcolepsy and cardiovascular disorders. Data were obtained from a pooled analysis of the HARMONY 1 (8-week) and HARMONY CTP (7-week) clinical trials and from the 12-month, open-label

HARMONY 3 trial. The pooled analysis included 166 patients (pitolisant, n=85; placebo, n=81). Mean change in heart rate from baseline to end-of-treatment was -0.5 beats/min with pitolisant and -0.2 beats/min with placebo (LS mean difference, -0.4; p=0.744). Mean change was also similar for pitolisant versus placebo in systolic (LS mean difference, 0.0; p=0.983) and diastolic (LS mean difference, -0.6; p=0.552) blood pressure, as was mean change in QTc interval (LS mean difference, 0.4; p=0.911). Cardiac adverse events with pitolisant included heart rate increase (n=4), right bundle branch block (n=1), sinus tachycardia (n=1), and palpitations (n=1), and with placebo included blood pressure increase (n=1). In the long-term study, mean change from baseline in QTc interval was 3.1 msec at Month 6 (n=70) and 6.1 msec at Month 12 (n=67); three patients had a post-baseline increase >60 msec but none had QTc >500 msec. Based on this analysis, no cardiac safety signals were observed during treatment with pitolisant administered up to the maximum dose of 35.6 mg and for up to one year.

Potential New Indications for Pitolisant

We are actively working on label expansion for WAKIX in narcolepsy, including indications for both EDS and cataplexy in pediatric patients. We also intend to work with the FDA toward gaining pediatric exclusivity for WAKIX. We believe that pitolisant's ability to regulate histamine and histaminergic signaling gives it the potential to provide therapeutic benefit in other disorders that are mediated through the H_3 receptor and histamine signaling and offers a *portfolio in a product* opportunity with pitolisant. Histamine plays an important role in normal physiologic functioning beyond wakefulness in the areas of attention, vigilance, behavior and cognition. The presence of H_3 receptors in the hypothalamus, brainstem and cerebral cortex account for different functions, which could provide an opportunity for pitolisant to treat symptoms other than EDS in different disorders. In addition, H_3 receptors are located mainly in the CNS as opposed to other parts of the body outside the CNS. This fact, along with pitolisant being highly selective for the H_3 receptor (as opposed to H_1 receptors, H_2 receptors and H_4 receptors), is the reason we believe in pitolisant's unique MOA and its potential to improve symptoms in patients living with rare neurological disorders, in which impaired histamine signaling is part of the underlying pathophysiology.

- Role of histamine in normal physiologic functioning beyond wake promotion (e.g. attention, vigilance, behavior, cognition)
- Location of H_3 receptors in hypothalamus, brainstem, and cerebral cortex account for different functions (and potential symptoms in different disorders)
- Limited H_3 receptor populations outside the CNS



Our initial plan is to seek new indications in patient populations that have symptom overlap with narcolepsy, such as EDS, while potentially pursuing opportunities in other CNS disorders of hypersomnolence. The initial clinical targets will focus on rare neurological disorders consistent with our overall strategy. We submitted an IND for PWS in October 2019 and received acknowledgement from the FDA that the proposed clinical investigation may proceed. We subsequently completed a Phase 1 PK clinical trial in pediatric patients with PWS in the fourth quarter of 2019, and initiated a long-term, open-label safety trial in these patients. In December 2020, we initiated a

Phase 2 clinical trial to evaluate pitolisant for the treatment of EDS and other key symptoms in patients with PWS and anticipate topline results from this trial in the first half of 2022. We submitted an IND for DM at the end of 2020 and the IND opened in January 2021, after which we received a "Study May Proceed" letter from the FDA in February 2021. We plan to initiate a Phase 2 clinical trial in patients with DM1 during the first half of 2021, and anticipate topline results in the second half of 2022. While conducting clinical programs to evaluate these indications, other clinical endpoints beyond EDS will be evaluated as secondary or exploratory endpoints, such as behavioral symptoms, vigilance, fatigue and cognition, to broaden the investigation of pitolisant with the hope of generating pilot data to help inform the next phase of our clinical development strategy.

Label Expansion in Narcolepsy

Cataplexy Indication

The NDA submission for WAKIX initially sought approval for the treatment of both EDS and cataplexy in adult patients with narcolepsy. Our application requesting approval for a cataplexy indication was based on the cataplexy results from HARMONY CTP and HARMONY 1. The FDA approved WAKIX for the treatment of EDS in adult patients with narcolepsy but issued a CRL for the cataplexy indication, . The FDA determined that, although we had submitted one positive clinical trial for cataplexy (HARMONY CTP), the NDA submission did not provide substantial evidence of effectiveness regarding cataplexy. The FDA therefore recommended that we conduct a second trial substantiating the results of HARMONY CTP in order to obtain approval for the cataplexy indication.

We attended a Type A post-CRL meeting with the FDA on December 12, 2019 to discuss the cataplexy indication, during which we pointed the FDA to additional analyses that were conducted in support of the HARMONY 1 cataplexy data and which were included in the NDA submission. Following additional interactions with the FDA, we received a general advice letter in June 2020 stating that the FDA had re-analyzed data from the HARMONY 1 clinical trial and confirmed that the cataplexy data from the HARMONY 1 clinical trial supported a statistically significant reduction in the daily rate of cataplexy in the pitolisant group when compared with the placebo group. As a result, the FDA recommended we submit a complete response resubmission in pursuit of the adult cataplexy indication for WAKIX, which we sent to the FDA in August 2020. On October 13, 2020 we received regulatory approval for WAKIX for the treatment of cataplexy in adult patients with narcolepsy.

Pediatric Narcolepsy

Approximately 5% of diagnosed narcolepsy patients (approximately 3,600 patients) are 19 years of age or under. Symptoms often have a more profound effect in children, resulting in reduced function and greater psychological impact. Until the fourth quarter of 2018, no treatments were approved for pediatric patients with narcolepsy, at which time Xyrem received an expanded indication for the treatment of cataplexy or EDS in patients seven years of age or older with narcolepsy. Xywav (low sodium formulation of Xyrem) received the same indication in July 2020. We intend to engage with the FDA in pursuit of pediatric exclusivity and commence a Phase 3 trial in pediatric patients in the second half of 2021 in pursuit of pediatric indications for both EDS and cataplexy. Our current plan is to evaluate approximately 90 to 100 pediatric patients, ages six to up to 18, to assess the safety and efficacy of pitolisant in pediatric narcolepsy patients on improvement in both EDS and reduction in cataplexy.

Develop Pitolisant in New Patient Populations in Pursuit of Additional Indications

Prader-Willi Syndrome

PWS is a rare genetic disorder caused by a loss of function of specific genes on chromosome 15 resulting in hypothalamic dysfunction and decreased levels of hypocretin in some patients with PWS. The hypothalamus controls both sleep-wake states and hunger-satiety; therefore, two of the main symptoms in patients with PWS are EDS and hyperphagia. Other features include low muscle tone, short stature, behavioral problems and cognitive impairment. It is estimated that approximately one in 15,000 to 20,000 people in the United States suffer from PWS, and over half of those suffering from PWS also have reported or experienced EDS. We submitted an IND for PWS in October 2019 and received acknowledgement from the FDA that the proposed clinical investigation may proceed. We subsequently completed a Phase 1 PK clinical trial in pediatric patients with PWS in the fourth quarter of 2019, and initiated a long-term, open-label safety trial in these patients. In December 2020, we initiated a Phase 2 clinical trial to evaluate pitolisant for the treatment of EDS and other key symptoms in patients with PWS and anticipate topline results from this trial in the first half of 2022.

PWS poses a heavy burden for both patients and caregivers and there are few therapeutic options available and no FDA-approved treatments for EDS in patients with PWS. Clinical development programs in PWS have focused on hyperphagia, with no other programs focusing on EDS or cognitive function. EDS is thought to have a negative effect on behavior and cognitive function and could exacerbate these symptoms in patients with PWS. In addition, impaired histamine signaling in the brain can contribute to behavioral symptoms and impaired cognition. We believe there is a compelling opportunity for the mechanism of action of pitolisant to impact the EDS component of this disorder as well as other symptoms, such as behavioral issues and cognitive impairment.

We have collaborated with the Foundation for Prader-Willi Research (the "FPWR") to advance our clinical program and underscore our commitment to this patient population. We are members of the FPWR Clinical Trials Consortium and are working with members of its Scientific Advisory Board to gain their insights for our development program. Progress to date includes (i) opening an IND for PWS in October 2019, (ii) the completion of a Phase 1 PK trial in patients with PWS in the fourth quarter of 2019, with patients actively rolling over into an open-label, long-term safety trial, (iii) the submission of a Phase 2 clinical protocol to the FDA for review and comment, and (iv) initiation of a Phase 2 trial in December 2020.

The Phase 2 clinical trial is a randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of pitolisant in patients with PWS ages 6 to 65. An estimated 60 to 70 patients will be enrolled at approximately 10 sites across the United States. Patients will be randomized to low-dose pitolisant, high-dose pitolisant or placebo in a 1:1:1 treatment ratio and titrated over three weeks up to their randomized dose, followed by eight weeks of stable dosing. The primary trial objective is to assess for improvement in EDS as measured by the Multiple Sleep Latency Test. Secondary endpoints include several behavioral symptom scales as well as specific measures of cognitive function using validated computer-based assessments. Clinician global impression of disease severity, caregiver global impression of EDS severity, and overall caregiver burden will be measured. Exploratory endpoints include the effect of pitolisant on hyperphagia and measurements of ghrelin levels. Patients who complete the trial will be eligible to participate in an open-label extension phase to assess the long-term safety and effectiveness of pitolisant in patients with PWS, which will run throughout the duration of the PWS development program.

Myotonic Dystrophy

DM is a rare, multi-system genetic disease that affects the neuromuscular system as well as several other systems. The primary symptom in patients with DM is myotonia, which is an impairment in the ability of muscles to relax; progressive muscle weakness is another prominent symptom of the disorder. It is inherited in an autosomal dominant pattern and there are two main types: DM1 and DM2. The underlying cause of DM1 is a mutation in the DMPK gene on chromosome 19. DM1 is the most common form of adult-onset muscular dystrophy and affects as many as 140,000 patients in the United States. EDS and fatigue are hallmark clinical characteristics in the majority of patients with DM1 and are referred to as the most frequent non-muscular symptoms in patients with DM1. EDS and fatigue occur in approximately 80% to 90% of patients with DM1. Cognitive impairment is also a prominent symptom in patients with DM1 and all of these symptoms are thought to be mediated through H_3 receptors and histaminergic pathways located throughout the CNS. DM2 is not as common as DM1 with an estimated prevalence of between 3,000 and 29,000 patients in the United States. The underlying cause of DM2 is a mutation in the CBNP gene on chromosome 3. Patients with DM1 and DM2 share similar phenotypes but disease onset is later in patients with DM2 and symptoms tend to be milder. There are currently no FDA-approved treatments for patients with DM, which represents a significant unmet medical need.

The therapeutic application of pitolisant may provide benefits across the key symptoms of EDS and fatigue which are often among the chief complaints of patients with DM. In a survey of 451 DM1 patients, daytime sleepiness and fatigue were second only to muscle weakness in symptom prevalence and impact. Our clinical program will be designed to demonstrate effect on measures of EDS and fatigue, as well as assess performance related to cognitive function, such as attention, vigilance and working memory. Progress to date includes working with key opinion leaders to develop the scientific rationale for the investigation of pitolisant in patients with DM, development of a Phase 2 clinical protocol, submission of an IND at the end of 2020, the opening of an IND in January 2021 and receipt of a "Study May Proceed" letter from the FDA in February 2021. We plan to initiate a Phase 2 clinical trial in patients with DM1 in the first half of 2021.

The proposed Phase 2 clinical trial is a randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of pitolisant in adult patients with DM ages 18 to 65. An estimated 130 to 140 patients will be enrolled at approximately 14 to 16 sites across the United States. Patients will be randomized to low-dose pitolisant, high-dose pitolisant, or placebo in a 1:1:1 treatment ratio and titrated over three weeks up to their randomized dose, followed by eight weeks of stable dosing. The primary trial objective is to assess for improvement in EDS as measured by the MWT and the ESS. Secondary endpoints include assessments of fatigue as well as specific measures of cognitive function using validated computer-based assessments. Clinician and patient global impression of disease severity using the CGI-S and PGI-S, respectively, will be measured as well as disease-specific patient assessments of overall disease burden. Plasma samples will be collected to generate pharmacokinetic data and a PK/PD analysis will be performed. Patients who complete the trial will be eligible to participate in an open-label extension phase to assess the long-term safety and effectiveness of pitolisant in patients with DM, which will run throughout the duration of the DM development program.

Other Potential Indications

The next phase of clinical development for pitolisant will be guided by the signals generated from the clinical trials described above and other potential trials in patients with PWS and DM. If we observe favorable results in these trials on the symptoms of fatigue and cognitive dysfunction, we plan to investigate pitolisant in other rare neurological patient populations in which these symptoms are a prominent part of the disease process and result in significant impact on daily functioning. Furthermore, we believe opportunities exist in adjacent disorders to narcolepsy, including other CNS disorders of hypersomnolence, which could lead to additional potential new indications.

Manufacturing, Supply and Distribution

We sell WAKIX to our customers, a limited number of specialty distributors, that, in turn, distribute WAKIX to patients.

We have secured a commercial drug supply to support the launch of WAKIX in the United States. Although we do not currently own or operate facilities for product manufacturing, storage and distribution, or testing, we have contracted directly with third parties for each of these functions.

Manufacturing is subject to extensive regulation that imposes various procedural and documentation requirements that govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, and more. Our systems and our contractors are required to be in compliance with these regulations, and compliance is assessed regularly through monitoring of performance and a formal audit program.

Our current supply chain for WAKIX involve several manufacturers that specialize in specific operations of the manufacturing process, specifically, intermediate and starting material manufacturing, drug substance manufacturing, and drug product manufacturing, labeling and secondary packaging, and distribution services:

- Interor S.A. manufactures our BF4 and BF6 intermediate and starting material used in the active pharmaceutical ingredient (“API”).
- Corden Pharma Chenôve SAS, a full-service contract development and manufacturing organization (“CDMO”) manufactures our API.
- Patheon UK Limited, a CDMO owned by Thermo Fisher Scientific Inc., manufactures our finished product tablets and fills them into unlabeled bottles.
- Carton Service, Inc., d/b/a Pharma Packaging Solutions, handles our labeling and secondary packaging.
- Integrated Commercialization Solutions, LLC (ICS), a division of AmerisourceBergen Corporation, is our third-party logistics provider.

- Inmar Rx Solutions, Inc., an advanced technology and data analytics company, specializes in reverse distribution of our product and manages our pharmaceutical returns and product recall, if needed.

Competition

Our industry is highly competitive and subject to rapid and significant change as research provides a deeper understanding of rare neurological disorders, including narcolepsy, and as new therapies are developed. We face potential competition from multiple sources, including large pharmaceutical, biotechnology and specialty pharmaceutical companies. The key competitive factors affecting the success of WAKIX, and any other product candidates that we develop, if approved, are likely to be efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

WAKIX competes with currently FDA-approved products for the treatment of EDS or cataplexy in adult patients with narcolepsy, all of which are controlled substances. Jazz Pharmaceuticals' Xyrem (sodium oxybate) is an FDA-approved product for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy Xyrem is a Schedule III controlled substance available only through a restricted access REMS program. Xywav, a lower sodium formulation of Xyrem, was approved in July 2020, (became commercially available in November 2020), and is also a Schedule III controlled substance subject to the same restricted access REMS program as Xyrem. Provigil and Nuvigil, which are Schedule IV WPAs, and stimulants such as methylphenidate and amphetamine (both Schedule II controlled substances), are approved for the treatment of EDS in narcolepsy. Anti-depressants and certain other agents are sometimes used off-label for the treatment of cataplexy in narcolepsy. Jazz Pharmaceuticals' Sunosi (solriamfetol) was approved by the FDA in March 2019 and launched in July 2019. Sunosi (solriamfetol) is a Schedule IV controlled substance and is indicated to improve wakefulness in adult patients with EDS associated with narcolepsy or obstructive sleep apnea. It is not indicated for cataplexy in patients with narcolepsy. Additionally, Avadel Pharmaceuticals is working on a once nightly formulation version of sodium oxybate, with approval expected in 2021 or beyond, and Xyrem is expected to go generic in 2023. Beyond 2023, there are other potential future competitive products in development, including Axsome Therapeutics's AXS-12 (reboxetine) product candidate and Takeda's TAK-925/994 (orexin 2 receptor agonist) product candidates.

We believe WAKIX offers a differentiated product profile that is competitive with each of the products listed above, some of which are only approved for EDS while others (Xyrem and Xywav) are approved for the treatment of both EDS or cataplexy in patients with narcolepsy. It should be noted that WAKIX has not been compared with these products in head-to-head clinical trials, but its non-scheduled status represents a distinct competitive advantage relative to those same products. Additionally, WAKIX is priced lower than Xyrem and Xywav, which we believe is a competitive advantage for WAKIX and may contribute to third-party payor preferences for WAKIX relative to Xyrem and Xywav. Conversely, WAKIX is priced higher than other competitors such as Provigil, Nuvigil, Sunosi and certain generic competitors, such as methylphenidate and amphetamine, which may contribute to third-party payor preferences for those lower-priced treatment options relative to WAKIX.

Customers and Suppliers

We depend on a few major customers. For the year ended December 31, 2020, three customers accounted for 100% of gross product revenues; Caremark LLC accounted for 40% of gross product revenues; PANTHERx Specialty Pharmacy LLC accounted for 33% of gross product revenues; and Accredo Health Group, Inc. accounted for 27% of gross product revenues. We also depend on a single source supplier for our product, product candidates and active pharmaceutical ingredient.

Strategic Agreement

License and Commercialization Agreement with Bioprojet

On July 28, 2017, we and Bioprojet entered into the Bioprojet License Agreement. Bioprojet granted to us an exclusive, sublicensable license to commercialize, in the United States and its territories, commonwealths, and protectorates, including Puerto Rico, a product containing pitolisant currently known as WAKIX for narcolepsy, obstructive sleep apnea, idiopathic hypersomnia, Parkinson's disease, and any other indication agreed upon by the parties (which currently include PWS and DM), or the field, as well as rights to related patent rights, know-how, trademarks, trade dress, regulatory filings and approvals (the "Bioprojet Assets"). Bioprojet also granted us a co-

exclusive (with Bioprojet), sublicensable license to Bioprojet Assets to clinically develop and register the pitolisant product in the field in the United States. Bioprojet retains the right to manufacture the product in the United States, and to develop outside the United States and commercialize other products that contain pitolisant as an active ingredient anywhere in the world. Bioprojet also granted us an exclusive license to use certain trademarks and trade names in connection with the commercialization of the product under the Bioprojet License Agreement.

Under the Bioprojet License Agreement, Bioprojet is responsible for conducting all preclinical studies and clinical trials necessary for achieving and maintaining regulatory approval in the United States for narcolepsy and cataplexy indications, including all costs and expenses. We are responsible for all other costs associated with other development and regulatory activities, unless Bioprojet otherwise agrees to participate in funding such activities. Bioprojet was responsible for filing, with our participation, the initial new drug application for the product with the FDA and Bioprojet did transfer such application to us upon approval by the FDA in accordance with the terms of the Bioprojet License Agreement.

Upon approval by the FDA, we were required under the Bioprojet License Agreement to promptly launch the product and use commercially reasonable efforts to commercialize the approved products in the United States in the field for each approved indication. In addition, we are required to deploy a number of sales representatives and spend an amount of expenditure, each as agreed upon in a commercialization plan.

Under the Bioprojet License Agreement, Bioprojet has the right and authority to prepare, file, prosecute and maintain all Bioprojet patents on a worldwide basis at its own cost. Bioprojet shall keep us informed of the course of prosecution and other proceedings in the United States. We have the first right to enforce the licensed patent rights with respect to any infringing products in the United States. If we do not bring an action to enforce such patents against infringing activities that involve such infringing products, Bioprojet has the right to bring such action.

We paid Bioprojet an initial license fee of $150.0 million, a milestone payment of $50.0 million upon FDA acceptance of the NDA in February 2019, and a milestone payment of $75.0 million plus an addition $2.0 million fee for approval of the NDA in November 2019. Upon the Cataplexy Milestone Trigger Date, we became obligated to make the Cataplexy Milestone Payment to Bioprojet pursuant to the terms of the Bioprojet License Agreement. Subsequently, in October 2020, we made a payment to Bioprojet of $2.0 million to extend the Cataplexy Milestone Payment due date to within 90 days of the Cataplexy Milestone Trigger Date. On January 6, 2021, we made the $100.0 million Cataplexy Milestone Payment in full to Bioprojet. In addition, we are subject to a milestone payment of $40.0 million upon the attainment of aggregate net sales of WAKIX in the United States of $500.0 million subsequent to the date of NDA approval by the FDA pursuant to the Bioprojet License Agreement. We agreed to pay royalties on the product at tiered royalty rates of 13% to 24% based on annual total net sales during the period commencing on first commercial sale of the product and ending on the latest of 10 years from first commercial sale of the product, expiration of all regulatory exclusivity, or expiration of the last Bioprojet patent covering the product. Such royalty payments are subject to reductions based on royalties paid to any third party in order for us to commercialize the product. We also agreed to pay royalties in consideration for a trademark license at a rate of 3% of net sales for 20 years after first commercial sale of the product. We further agreed to pay minimum royalties during the third through tenth year of the Bioprojet License Agreement if the product is approved for narcolepsy to the extent such minimum royalties exceed the royalties payable as described above, which minimum amounts were calculated based on sales materially below our sales forecast.

The Bioprojet License Agreement will continue until the expiration of the obligation to pay royalties with respect to the product. We and Bioprojet may each terminate the Bioprojet License Agreement for a material breach by the other party that remains uncured for 90 days. Bioprojet may terminate the Bioprojet License Agreement in its entirety if we or our sublicensees challenge the licensed patents. In addition, we and Bioprojet have the right to terminate the Bioprojet License Agreement upon the other party’s insolvency.

Intellectual Property

Intellectual property, including patents, trade secrets, trademarks and copyrights, is important to our business. Our commercial success depends in part on our ability to obtain and maintain proprietary intellectual property protection for our WAKIX product and potential future pitolisant-based products, as well as for future

product candidates and novel discoveries, product development technologies, and know-how. Our commercial success also depends in part on our ability to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to develop and maintain protection of our proprietary position by, among other methods, licensing or filing U.S. and foreign patents and applications relating to our technology, inventions, and improvements that are important to the development and implementation of our business.

Our patent portfolio comprises three U.S. patents exclusively licensed to us from Bioprojet. One U.S. patent, No. 8,207,197, has claims directed to a polymorph, i.e. a specific crystalline form, of pitolisant and, methods for preparing that polymorph of pitolisant, which is expected to expire in February 2029 without taking into consideration any possible patent term extension. A second U.S. patent, No. 8,486,947, has claims directed to methods of treating excessive daytime sleepiness by administering pitolisant, which is expected to expire in September 2029 without taking into consideration any possible patent term extension. With all applicable patent term adjustments available and granted to us, the term of the last-to-expire pitolisant-related patent in our portfolio extends to September 2029. We may receive additional patent term based on the patent term extension described below.

The term of individual patents in our portfolio depends upon the legal term of patents in the countries in which they are obtained. In the United States, the patent term is 20 years from the earliest date of filing a non-provisional patent application. The term of a U.S. patent may be eligible for patent term adjustment, which permits patent term restoration as compensation for delays incurred at the U.S. Patent and Trademark Office (the “USPTO”) during the patent prosecution process. In addition, for patents that cover an FDA-approved drug, the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Act”) permits a patent term extension of up to five years beyond the expiration of the patent. While the length of the patent term extension is related to the length of time the drug is under regulatory review, patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent per approved drug may be extended under the Hatch-Waxman Act. We have applied for patent term extension on two patents covering pitolisant, only one of which will receive patent term extension, if at all. While we have received confirmation from the USPTO that the patents are eligible for patent term extension, there is no guarantee that the applicable authorities, including the USPTO and the FDA, will agree with our assessment of whether such extension should be granted. We estimate the length of such extension to be 389 days; however, the USPTO, in conjunction with the FDA, will calculate the length of such extension and there is no guarantee that their calculation will align with our estimate.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Changes in either the patent laws or their interpretation in the United States may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, issued patents do not guarantee the right to practice our technology in relation to the commercialization of our products. Issued patents only allow us to block potential competitors from practicing the claimed inventions of the issued patents.

Further, patents and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that,

before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

We and/or our licensor also rely on protections under trade secret laws, and seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our trade secrets include, for example, certain program specific synthesis, formulations, patient selection strategies and certain aspects of our research. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us, and for employees and consultants to enter into invention assignment agreements with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Where applicable, the agreements provide that all inventions to which the individual contributed as an inventor shall be assigned to us, and as such, will become our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Further, we have in-licensed from Bioprojet the registered trademark product name "WAKIX" in the United States. We also have registered trademark protection in the United States for "KNOW NARCOLEPSY" as well as our brand and logo "HB," "HB HARMONY BIOSCIENCES" and "HARMONY BIOSCIENCES." We also have trademark applications pending with the U.S. Patent and Trademark Office for "REM AT THE WRONG TIME" and "NON-REM AT THE WRONG TIME."

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (the "FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP") requirements to establish the safety and efficacy of the proposed drug product for each indication;

- submission to the FDA of an NDA;

- satisfactory completion of an FDA advisory committee review, if applicable;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and

- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to commercial marketing or sale of the drug in the United States; and

- Compliance with any post-approval requirements, including the potential requirement to implement a REMS program or to conduct a post-approval study.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life. There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act ("PDUFA") guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision. Specifically, the FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety and quality.

The FDA also may require submission of a REMS to ensure that the benefits of the drug outweigh its risks. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

The Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

FDA Expedited Development and Review Programs

The FDA has various programs, including fast track designation, accelerated approval priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for

review and decision from the date of submission. Products that are eligible for fast track designation may also be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act ("FDASIA") passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. The designation includes all of the benefits of a fast track designation. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later

discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warning or other safety information about the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA") or an NDA submitted under Section 505(b)(2) ("505(b)(2) NDA") submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that (i) affects fewer than 200,000 individuals in the United States, or (ii) if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the product available in the United States for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants an orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Among other benefits of an orphan drug designation are tax credits for certain research and a waiver of the user fee for the NDA.

Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

We received an orphan designation for pitolisant for the treatment of narcolepsy and, upon approval of WAKIX, we received orphan exclusivity until 2026.

DEA Regulation

The Controlled Substances Act of 1970 ("CSA") establishes registration, security, recordkeeping, reporting, storage, distribution and other requirements administered by the DEA. The DEA is concerned with the control of handlers of controlled substances, and with the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. The FDA did not recommend that the DEA schedule WAKIX as a controlled substance, and WAKIX is therefore not scheduled as a controlled substance by the DEA.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. To meet its responsibilities, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Individual states also regulate controlled substances.

Other Healthcare Laws

In addition to FDA regulation of pharmaceutical products, pharmaceutical companies are subject to federal healthcare laws and regulations as well as regulation by the states and foreign jurisdictions in which they conduct their business that restrict business practices in the pharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we market, sell and distribute our products for which we obtain marketing approval. These laws include U.S. federal and state anti-kickback and false claims laws, civil monetary penalties laws, consumer protection and transparency laws as well as similar foreign laws in the jurisdictions outside the U.S., including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation.

The federal civil and criminal false claims laws, including the civil False Claims Act, prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act and the civil monetary penalties statute. The False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the False Claims Act and to share in any monetary recovery.

The federal Civil Monetary Penalties Law prohibits, among other things, the offering or transferring of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular supplier of Medicare or Medicaid payable items or services. Federal government price reporting laws require manufacturers to calculate and report complex pricing metrics to government programs.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, these reporting obligations will extend to include payments and transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified nurse midwives.

Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing information and marketing expenditures or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; and state and local laws that require the registration of pharmaceutical sales representatives.

Violation of any of such laws or any other governmental regulations that apply may result in significant criminal, civil and administrative penalties including damages, fines, imprisonment, disgorgement, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, implementation of corporate compliance programs, and reporting of payments or transfers of value to healthcare professionals.

Data Privacy and Security Laws

Pharmaceutical companies may be subject to U.S. federal and state health information privacy, security and data breach notification laws, which may govern the collection, use, disclosure and protection of health-related and other personal information. In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to the Department of Health and Human Services ("HHS"), affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information ("PHI"), a complaint about privacy practices or an audit by the HHS may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act ("FTCA"). The FTC expects

a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which may be more stringent, broader in scope or offer greater individual rights with respect to PHI than HIPAA, many of which may differ from each other, thus, complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act ("CCPA"), which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act (the "CPRA") recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required.

In Europe, the General Data Protection Regulation ("GDPR"), went into effect in May 2018 and imposes stringent data protection requirements for controllers and processors of personal data of persons within the European Economic Area ("EEA"). The GDPR applies to any company established in the EEA as well as to those outside the EEA if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or the monitoring of their behavior. The GDPR, together with national legislation, regulations and guidelines of the EEA member states and the United Kingdom governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA or the United Kingdom, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for breaches of the data protection obligations. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Further, from January 1, 2021, companies have to comply with the GDPR and also the United Kingdom GDPR ("UK GDPR") which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. Currently there is a four to six-month grace period agreed in the EU and United Kingdom Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. However, it is not clear whether (and when) an adequacy decision may be granted by the European Commission enabling data transfers from EU member states to the United Kingdom long term without additional measures. These changes may lead to additional costs and increase our overall risk exposure. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and

managed healthcare organizations, and the level of reimbursement for such product by third-party payors. In the United States, no uniform policy exists for coverage and reimbursement for pharmaceutical products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. The process for determining whether a third-party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service and the level of coverage and reimbursement can differ significantly from payor to payor. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. Furthermore, there can be no assurance that a product will be considered medically reasonable and necessary for a specific indication, that a product will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability to sell a product profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the ACA was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States and significantly affected the pharmaceutical industry. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (increased to 70 percent pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected expanded the types of entities eligible for the 340B drug discount program; expanded eligibility criteria for Medicaid programs; creates a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional legislative challenges to certain aspects of the ACA. The U.S. Supreme Court is currently reviewing the constitutionality of the ACA in its entirety, although it is unclear how the Supreme Court will rule. Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal

year, which was temporarily suspended from May 1, 2020 through March 31, 2021 under the Coronavirus Aid, Relief and Economic Security Act ("CARES Act"), and reduced payments to several types of Medicare providers.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products in an attempt to control drug costs. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressures.

Facilities

Our corporate headquarters are located 630 W. Germantown Pike Plymouth Meeting, Pennsylvania. In December 2020, we leased additional office space at this same location, which increased our footprint to approximately 28,638 square feet of office space. As of December 31, 2020, approximately 40 of our employees are located at our corporate headquarters. Pursuant to our Right of Use Agreement with Paragon, we also utilize office space at 330 N. Wabash Ave, Suite 3500, Chicago, Illinois 60611, where approximately 10 of our employees are located.

Human Capital Management

As of December 31, 2020, we have approximately 150 full-time employees, 100 of whom are dedicated to commercial functions, which includes sales, marketing, market access, commercial operations and insights, and 25 of whom are dedicated to research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off.

We believe that much of our success is rooted in the diversity of our teams and our commitment to inclusion. We value diversity at all levels and focus on extending our diversity and inclusion initiatives across our entire workforce.

Corporate Social Responsibility

Social responsibility has always been integral to our core values. We are committed to doing business with integrity and ethics. We focus on providing our employees safe and healthy working conditions, and actively participate in the communities where we are located. In addition, we support philanthropic organizations, patient-focused associations, local and national charitable organizations, and areas of need across the country by providing monetary donations or supplying food, medical supplies and other resources. We collaborate with patient advocacy organizations to understand the needs of patients living with rare, neurological disorders including narcolepsy, and are committed to addressing those needs.

Corporate Information

Our operating subsidiary, Harmony Biosciences, LLC, was formed in May 2017. We were formed in July 2017 as Harmony Biosciences II, LLC, a Delaware limited liability company, and we converted to a Delaware corporation named Harmony Biosciences II, Inc. in September 2017. In February 2020, we changed our name to Harmony Biosciences Holdings, Inc. Our principal executive offices are located at 630 W. Germantown Pike, Plymouth Meeting, PA 19462, and our telephone number is (484) 539-9800. Our internet website is www.harmonybiosciences.com. We routinely make available important information free of charge, including copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after such reports are electronically filed with, or furnished to, the SEC. We recognize our website as a key channel of distribution to reach public investors and as a means of disclosing material non-public information to comply with our disclosure obligations under SEC Regulation FD. Information contained on our website shall not be deemed incorporated into, or to be part of this Annual Report on Form 10-K, and any website references are not intended to be made through active hyperlinks.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below and the other information included or incorporated by reference in this Annual Report on Form 10-K before making an investment in our common stock. Our business, financial condition, results of operations, or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. See "Part I—Cautionary Note Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

Risks Related to Our Financial Condition and Capital Requirements

We have incurred significant losses since our inception, expect to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or fail to become commercially viable. We have only recently begun to generate revenue from product sales and have incurred losses in each year since our inception for most periods. Our ability to generate revenue and achieve profitability depends on our ability to successfully commercialize WAKIX for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, and to successfully develop and obtain the regulatory approvals necessary to commercialize pitolisant for other indications. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we commercialize WAKIX and as we continue to develop and potentially commercialize pitolisant for other indications.

We have only recently begun generating revenue from product sales and may never be profitable.

Other than WAKIX, we do not currently have any products that are available for commercial sale, and we may never achieve profitability. Our net loss was $36.9 million and $152.0 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $488.2 million. Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue until we further commercialize WAKIX and/or and obtain regulatory approval for potential additional indications for pitolisant. We generated net product revenues of $159.7 million and $6.0 million for the years ended December 31, 2020 and 2019, respectively. Successful commercialization will require achievement of many key milestones, including demonstrating safety and efficacy in clinical trials, obtaining regulatory approval, including marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any further losses or if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable may depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

We have a limited operating history and history of commercializing drugs, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2017, and our operations to date have been largely focused on staffing our company, business planning, raising capital, acquiring the rights to pitolisant, seeking registration in the United States for our product WAKIX, which is approved for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, the commercialization of WAKIX, manufacturing WAKIX on a commercial scale, and preparing to develop pitolisant for other potential indications. This has

included preparing the application for regulatory approval and other activities that were required for us to obtain approval of our NDA, and activities related to commercializing WAKIX. WAKIX is our only drug candidate for which we have obtained regulatory approval. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a longer history of successfully developing and commercializing drugs.

We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors.

We have only limited capital and may need to raise additional capital before we become profitable.

As of December 31, 2020, we had an accumulated deficit of $488.2 million, and available cash and cash equivalents and restricted cash of $229.4 million. We have $194.3 million of debt outstanding under our Credit Agreement with OrbiMed. We believe that our anticipated cash from operating and financing activities and existing cash and cash equivalents will enable us to meet its operational liquidity needs and fund our planned investing activities for the next twelve months.

This estimate is based on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Because the length of time and activities associated with the successful development of our product candidates is highly uncertain, we are unable to estimate with certainty the actual funds we will require for development and any approved marketing and commercialization activities.

To fund future operations to the point at which we are able to generate positive cash flow from sales of WAKIX or other potential product candidates, we may need to raise significant additional capital. The amount and timing of future funding requirements will depend on many factors, including, but not limited to:

- the results of our commercialization of WAKIX;
- the cost of sales, marketing and distribution capabilities for our product candidates in regions where those product candidates are approved and where we choose to commercialize our products on our own;
- the effect of competing technological and market developments;
- the cost and timing of manufacturing activities;
- the payment of royalties and milestone payments to Bioprojet;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other regulatory authorities;
- the willingness of the FDA and other comparable regulatory authorities to accept our clinical trial designs, as well as data from our completed and planned clinical trials and preclinical studies and other work, as the basis for the review and approval of pitolisant for other potential indications or of any other product candidates;
- the potential expansion of our current development programs to seek new indications for pitolisant, potential new development programs for additional indications, and related general and administrative support;
- the initiation, progress, timing, and results of our clinical trials through all phases of development for pitolisant as a treatment for other indications and any other product candidates;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights, in-licensed or otherwise;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us for pitolisant or future product candidates;
- the cost of acquiring rights to other pharmaceutical products in the future to further develop and commercialize;

- the cost of general operating expenses; and
- the costs of operating as a public company.

We have no committed source of additional capital and we anticipate that we may seek to fund our operations through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. We cannot assure you that anticipated additional financing will be available to us on favorable terms, or at all. Although we have been successful in obtaining financing through the issuance of our equity securities and debt facilities, we cannot assure you that we will be able to do so in the future. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us to fund our commercialization of WAKIX and clinical development and commercialization of pitolisant for other indications, if approved, and other business activities, we could be forced to significantly delay, scale back, or discontinue the development or commercialization of our product candidates or curtail or cease our operations.

Raising additional funds by issuing securities may cause dilution to existing shareholders, raising additional funds through debt financings may involve restrictive covenants, and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights to our technologies or product candidates.

We expect that significant additional capital will be needed in the future to continue our planned operations. Until such time, if ever, that we can generate sufficient product revenue from the sale of WAKIX, we may need to finance our cash needs through a combination of equity offerings, debt financings, including our Credit Agreement, strategic alliances and license and development agreements or other collaborations. To the extent that we raise additional capital by issuing equity securities, our existing shareholders' ownership may experience substantial dilution, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of a common shareholder. Additionally, any agreements for future debt or preferred equity financings, if available, may involve covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely affect our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

Our auditor has previously expressed substantial doubt about our ability to continue as a going concern and we may be unable to remain a going concern.

In light of our recurring losses, accumulated deficit and negative cash flow as described in our notes to our consolidated financial statements, we had previously concluded there was substantial doubt regarding our ability to continue as a going concern and the report of our independent registered public accounting firm on our financial statements for the year ended December 31, 2019 contained an explanatory paragraph communicating this matter. Our financial statements did not include any adjustments that may have been necessary in the event we were unable to continue as a going concern. Had we been unable to establish to the satisfaction of our independent registered public accounting firm that our expected operational performance and liquidity would be sufficient to allow for the removal of this going concern qualification, we would have needed to significantly modify our operational plans for us to continue as a going concern. We believe that our anticipated cash from operating and financing activities and existing cash and cash equivalents, will enable us to meet our operational liquidity needs and fund our planned investing activities for the next twelve months.

We have made and may be required in the future to make significant payments to Bioprojet under our licensing and collaboration agreements for pitolisant.

Under our agreements with Bioprojet, we are subject to significant obligations, including payment obligations upon the achievement of specified milestones and payments based on product sales, as well as other material obligations. Certain of the milestone payments payable by us under these agreements were paid prior to our commercialization of WAKIX.

Upon the Cataplexy Milestone Trigger Date, we became obligated to make the $100.0 million Cataplexy Milestone Payment to Bioprojet pursuant to the terms of the Bioprojet License Agreement. Subsequently, in October 2020, we made a payment to Bioprojet of $2.0 million to extend the Cataplexy Milestone Payment due date to within 90 days of the Cataplexy Milestone Trigger Date. On January 6, 2021, we made the $100.0 million Cataplexy Milestone Payment in full to Bioprojet. In addition, we are subject to a milestone payment of $40.0 million upon the attainment of aggregate net sales of WAKIX in the United States of $500.0 million subsequent to the date of NDA approval by the FDA pursuant to the Bioprojet License Agreement.

There can be no assurance that we will have the funds necessary to make such payments in the future, or be able to raise such funds when needed, on terms acceptable to us, or at all. If we fail to comply with our payment obligations, Bioprojet has the right to terminate the license agreement, in which event we would not be able to develop, manufacture or market WAKIX or any other pitolisant-based product candidate. Furthermore, if we are forced to raise additional funds to make such payments, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

Our ability to utilize our net operating loss carryforwards may be limited.

As of December 31, 2020, we had U.S. federal and state net operating loss carryforwards of approximately $159.4 million and $157.7 million, respectively. As of December 31, 2019, we had U.S. federal and state net operating loss carryforwards of approximately $147.8 million and $139.3 million, respectively. Our ability to utilize our federal net operating loss carryforwards may be limited under Section 382 of the Internal Revenue Code of 1986, as amended (the “Code”). The limitations apply if we experience an “ownership change,” which is generally defined as a greater than 50 percentage point change (by value) in the ownership of our equity by certain stockholders over a rolling three-year period. Similar provisions of state tax law may also apply to limit the use of our state net operating loss carryforwards. We have not assessed whether such an ownership change has previously occurred. If we have experienced an ownership change at any time since our incorporation, we may already be subject to limitations on our ability to utilize our existing net operating loss carryforwards to offset taxable income. In addition, future changes in our stock ownership, which may be outside of our control, may trigger an ownership change and, consequently, the limitations under Section 382 of the Code. As a result, if or when we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset such taxable income may be subject to limitations, which could adversely affect our future cash flows.

Our credit agreement contains restrictive and financial covenants that may limit our operating flexibility.

Our Credit Agreement with OrbiMed contains certain restrictive covenants that either limit our ability to, or require a mandatory prepayment in the event that, we engage in new lines of business, incur additional indebtedness or liens, make certain investments, make certain payments, pay cash dividends, merge with other companies or consummate certain changes of control, acquire other companies, transfer or dispose of certain assets, liquidate or dissolve, amend certain material agreements, enter into sale and leaseback transactions, enter into various other specified transactions, or change our name, location, executive office or executive management without notice. We, therefore, may not be able to engage in any of the foregoing transactions unless we obtain the consent of OrbiMed or prepay the outstanding amount under the Credit Agreement. The Credit Agreement also contains certain financial covenants, including minimum revenue and cash balance requirements (which include maintaining minimum liquidity of $12.5 million), and financial reporting requirements.

Our obligations under the Credit Agreement are secured by all of our property, with certain exceptions. We may not be able to generate sufficient cash flow or sales to meet the financial covenants or pay the principal and interest under the Credit Agreement. Furthermore, our future working capital, borrowings or equity financing could be unavailable to repay or refinance the amounts outstanding under the Credit Agreement. In the event of a liquidation, OrbiMed would be repaid all outstanding principal and interest prior to distribution of assets to unsecured creditors, and the holders of our common stock would receive a portion of any liquidation proceeds only if all of our creditors then existing, including OrbiMed, were first repaid in full.

Risks Related to Our Business

We are substantially dependent on our ability to successfully commercialize WAKIX, which is currently our only approved product. If we are unable to successfully commercialize WAKIX, our ability to generate revenue and our financial condition will be adversely affected.

Since our inception, we have invested substantially all of our capital resources on the development, registration and commercialization of WAKIX, which was approved for the treatment of EDS in adult patients with narcolepsy in August 2019 and for the treatment of cataplexy in adult patients with narcolepsy in October 2020. We cannot be certain that WAKIX will be successfully commercialized.

Our ability to generate revenue from product sales depends heavily on our success in many areas, including but not limited to:

- successfully commercializing WAKIX, either independently or with marketing service providers;
- the effectiveness of our sales and marketing strategy and operations, and obtaining market acceptance of WAKIX, including garnering market share from existing and future treatment alternatives;
- maintaining compliance with all regulatory requirements applicable to WAKIX and our commercial activities, including the post-marketing requirements and post-marketing commitments required by the FDA;
- obtaining coverage and adequate reimbursement from third-party payors for each of our product candidates;
- the continued acceptability of the safety profile of WAKIX and the occurrence of any unexpected side effects, adverse reactions or misuse, including potential business impact such as the need to withdraw the product (either voluntarily or as mandated by the FDA), loss of support by the advocacy communities or loss of positive corporate reputation resulting in related unfavorable media coverage in these areas;
- successfully managing third-party service providers involved in the manufacturing and development of pitolisant;
- successfully completing the development of pitolisant in other indications by demonstrating safety, tolerability and efficacy profiles that are satisfactory to the FDA;
- obtaining regulatory approvals to market pitolisant for other indications;
- complying with the terms of the license agreement with Bioprojet;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding the portfolio of intellectual property rights, including patents, trade secrets and knowhow; and
- attracting, hiring and retaining qualified personnel.

In our efforts to market WAKIX for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, our revenue will be dependent, in part, on the size of the markets in the United States, or in other territories where we may seek and obtain regulatory approval, the number of competitors in such markets, the acceptance of the price of the product in those markets and the ability to obtain reimbursement at any price. If the number of our addressable patients is not as large as we estimate or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products. If we are not able to generate substantial revenue from the sale of approved products, we may never become profitable.

The commercial adoption of WAKIX and any other product candidates we develop will depend on the degree of their market acceptance.

Even with the requisite approvals from the FDA and other regulatory authorities, the commercial adoption of WAKIX for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, and any other indications and product candidates we may develop, will depend on the degree of their acceptance by physicians, patients, third-party payors and others in the medical community. If WAKIX or any other product candidates we develop do not achieve an adequate level of market acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of WAKIX or any other product candidates we develop, if approved for commercial sale, will depend on a number of factors, some of which are beyond our control, including:

- the safety and efficacy of the product as demonstrated in clinical trials;
- the perception of physicians, patients, third-party payors and others in the medical community of the relative safety, efficacy, convenience, effect on quality-of-life and cost-effectiveness of the product, compared to those of other available treatments;
- the product's approved labeling, including the description of the product's approved indications, the description of its efficacy, including the endpoints in which it showed an improvement, and the prevalence and severity of any side effects, including any associated limitations or warnings;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to differentiate WAKIX or other approved products from other treatments in the same space;
- the adoption of WAKIX as a first-line therapy for EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy;
- the prevalence and severity of any side effects, including those that may be discovered following approval and commercialization;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- the publicity concerning our products or competing products and treatments;
- product liability litigation alleging injuries relating to our products or similar classes of drugs;
- any post-approval study requirements for our products and the results thereof; and
- sufficient third-party insurance coverage and reimbursement.

Our continuing efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits and risks of WAKIX may require significant resources and may never be successful. The adoption of WAKIX could be limited if physicians prescribe it only as a second line therapy. Physicians may opt to prescribe the products of our competitors for a variety of reasons. For example, WAKIX did not demonstrate non-inferiority to modafinil and, as such, physicians and patients may choose modafinil rather than WAKIX. Furthermore, because the clinical response to WAKIX may take several weeks before addressing EDS and cataplexy symptoms, patients and physicians may choose other fast acting, stimulant and wake promoting agents over WAKIX. If WAKIX fails to achieve an adequate level of acceptance by physicians, patients, third-party payors and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

We cannot guarantee that WAKIX or any other product candidates we may seek to develop will ever be commercially successful, and to the extent they are not commercially successful, such product candidates would incur significant expense with no corresponding revenue. Because we expect the sales of WAKIX to

generate substantially all of our revenue for the foreseeable future, the failure of WAKIX to find market acceptance would substantially harm our business and could require us to seek additional financing.

The market opportunity for WAKIX or any future product candidate we develop may be smaller than we estimate.

The potential market opportunity for WAKIX and any future product candidate is difficult to precisely estimate. Our estimates of the potential market opportunity for our product candidates include several key assumptions of the current market size and current pricing for commercially available products and are based on industry and market data obtained from industry publications, studies conducted by us, our industry knowledge, third-party research reports and other surveys. While we believe our estimates are reasonable and reliable, they may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of diseases and disorders. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for WAKIX or any future product candidate we develop may be limited or may not be amenable to treatment with WAKIX or such future product candidate, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business.

We rely on our license agreement with Bioprojet to provide rights to the core intellectual property relating to pitolisant, and any termination or loss of significant rights under the agreement would adversely affect our development and/or commercialization of pitolisant.

We have licensed our core intellectual property relating to pitolisant from Bioprojet. If, for any reason, our license and commercialization agreement with Bioprojet is terminated or we otherwise lose those rights, it would materially adversely affect our business. Pursuant to our license and commercialization agreement, we obtained intellectual property rights in connection with the commercialization of pitolisant in the United States and its territories, commonwealths and protectorates, including Puerto Rico, which includes an exclusive license to use certain intellectual property owned by Bioprojet related to clinically developing and commercializing the pitolisant product candidate for narcolepsy, obstructive sleep apnea, idiopathic hypersomnia and Parkinson's Disease.

Under the license agreement, Bioprojet is responsible for conducting all preclinical studies and clinical trials necessary for achieving and maintaining regulatory approval in the United States for narcolepsy and cataplexy indications, including all costs and expenses. We are responsible for all other costs associated with other development and regulatory activities, unless Bioprojet otherwise agrees to participate in funding such activities. We must obtain consent from Bioprojet before commencing any clinical trials related to pitolisant. Our ability to pursue indications other than the ones specifically enumerated in the license agreement is also contingent on mutual agreement of Bioprojet and us as to those indications and such agreement may be withheld at Bioprojet's discretion. If Bioprojet denies consent for us to conduct clinical trials or pursue any such other indication for any reason, we will not have the right under our license and commercialization agreement to commercialize our product for such indication. In such event, Bioprojet may pursue commercialization of such indication for itself in our territory, or it may license the right to commercialize such indication in our territory to third parties, including our competitors.

Our license and commercialization agreement also imposes on us obligations relating to exclusivity, territorial rights, development, commercialization, funding, payment, diligence, sublicensing, insurance, intellectual property protection and other matters. If we breach any material obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages to Bioprojet, and Bioprojet may have the right to terminate our license, which would result in us being unable to develop, manufacture and sell pitolisant and would materially adversely affect our business.

The ongoing COVID-19 pandemic may result in disruptions to our commercialization, clinical trials, manufacturing and other business operations, which could have a material adverse effect on our business, financial condition, operating results, cash flows and prospects.

The outbreak of COVID-19, which has been declared a global pandemic by the World Health Organization, has spread across the globe and is impacting worldwide economic activity. A public health epidemic, including COVID-19, poses the risk that we or our employees, contractors, suppliers, distributors and other partners, as well as physicians treating narcolepsy patients, may be prevented from conducting business and patient-care activities for an indefinite period of time, including due to shutdowns and quarantines that may be requested or mandated by governmental authorities. Beginning in March 2020, we transitioned our field-

based sales, market access, and medical employees to remote work and suspended work-related travel and in-person customer interactions with healthcare professionals and customers. Some of these activities have resumed in moderation following the establishment of proper protocols and procedures as COVID-19 restrictions have been revised. Our increased reliance on personnel working from home may negatively impact productivity or disrupt, delay or otherwise adversely impact our business. In addition, remote working could increase our cyber security risk.

General protective measures put into place at various governmental levels, including quarantines, travel restrictions and business shutdowns, may also negatively affect our operations. The responses to the COVID-19 pandemic may have had an impact on demand for WAKIX as a result of a reduced ability of prescribers to diagnose narcolepsy patients given the limitations in access to sleep testing, the reduced ability to see patients due to cancelled appointments and the reprioritization of healthcare resources toward treating COVID-19. The COVID-19 pandemic has affected our ability to access HCPs, and has caused fewer patients visits to their HCP, resulting in fewer prescriptions being written. The COVID-19 pandemic is leading to high unemployment and corresponding loss of insurance, resulting in more eligible patients taking advantage of patient assistance and/or free good programs, which is impacting our ability to convert demand to revenue and the corresponding revenue growth rate in possible future quarters will be adversely impacted by the ongoing COVID-19 pandemic.

The continued spread of COVID-19 and the measures taken by the governments of countries affected, particularly the United States and France, could also disrupt the supply chain and the manufacture or shipment of WAKIX and of drug substance and finished drug product. For example, we may face supply chain and manufacturing limitations or difficulties as resources are shifted toward vaccine manufacturing and distribution. Any delays or interruptions in the manufacture and supply of WAKIX could result in delays for our planned clinical trials, impair our ability to meet demand for new WAKIX prescriptions and impede our clinical trial recruitment, testing, monitoring, data collection and analysis and other related activities.

Any of the foregoing factors could have a material adverse impact on our business, financial condition, operating results, cash flows and prospects. The extent to which COVID-19 impacts our operations and those of our third-party partners will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, additional or modified government actions, new information which emerges concerning the severity of COVID-19 and the actions taken to contain the virus or treat its impact, among others. In particular, the speed of the continued spread of COVID-19 globally, and the magnitude of interventions to contain the spread of the virus, will determine the impact of the pandemic on our operations.

We may not be successful in our efforts to identify, in-license or acquire, discover, develop or commercialize additional product candidates, or identify other indications for pitolisant beyond EDS or cataplexy in adult patients with narcolepsy.

Although a substantial amount of our effort will focus on the commercialization of WAKIX for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, we also may seek to identify, in-license or acquire, discover, develop and commercialize additional product candidates in the rare neurological disorders field, and to identify other indications for pitolisant beyond the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy. We cannot assure you that our efforts to do so will be successful. Even if we are successful at in-licensing or acquiring additional product candidates, their requisite development activities may require substantial resources, and we cannot assure you that these development activities will result in regulatory approvals. We also cannot assure you that our efforts to develop and commercialize pitolisant for other indications beyond the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy will be successful.

Our business, products or product pricing could be subject to negative publicity, which could have a material adverse effect on our reputation, business, financial position, results of operations, liquidity and cash flows.

In recent years, the pharmaceutical industry has been the subject of public complaints and significant publicity regarding the pricing of pharmaceutical products, including publicity and pressure resulting from prices charged by competitors and peer companies for new products as well as price increases by competitors and peer companies on older products that the public has deemed excessive. We may experience downward pricing pressure on the price of WAKIX and any other future approved products due to social or political pressure to lower the cost of drugs, which could reduce our revenue and future profitability. Orphan drugs in particular have received recent negative publicity for the perceived high prices charged for them by their manufacturers, and as a result orphan drug developers such as us may be negatively impacted by such publicity

and any U.S. or other government regulatory response. Due to these factors, we may suffer public criticism and negative publicity in media coverage, by industry trade associations and legislators.

Any of the events or developments described above could result in reputational harm and reduced market acceptance and demand for our products, could harm our ability to market our products in the future, could cause us to incur significant expense, could cause our senior management to be distracted from execution of our business strategy, and could have a material adverse effect on our business, reputation, financial condition, results of operations, liquidity, cash flows and/or share price.

Third-party relationships are important to our business. If we are unable to enter into and maintain strategic collaborations or if these relationships are not successful, our business could be adversely affected.

We have limited product development and distribution capabilities and we do not yet have any product manufacturing capabilities. In addition, we may enter into collaborations for the development and commercialization of certain of our product candidates. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. Relationships we enter into may pose a number of risks, including the following:

- current or future third parties have, and future third-party collaborators may have, significant discretion in determining the efforts and resources that they will apply;
- third parties may not perform their obligations as expected;
- third parties may not pursue development and commercialization of any product candidates that we decide to develop as drugs and that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical study or trial results, changes in the third parties' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- third parties may delay preclinical studies or clinical trials, provide insufficient funding for a preclinical study or clinical trial, stop a preclinical study or clinical trial or abandon one of our product candidates, repeat or conduct clinical studies or new clinical trials or require a new formulation of a product candidate for clinical testing;
- third parties could independently develop, or develop with other third parties, products that compete directly or indirectly with our products and product candidates if the third parties believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our current or future collaborators as competitive with their own product candidates or products, which may cause such third parties to cease to devote resources to the commercialization of our product candidates;
- third parties may fail to comply with applicable regulatory requirements regarding the development, manufacture, packaging, labeling, holding, distribution and/or marketing of a product candidate or product;
- third parties with marketing and distribution rights to pitolisant or any future product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with third parties, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of pitolisant or any future product candidates, might lead to additional responsibilities for us with respect to pitolisant or any future product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- third parties may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- third parties may infringe the intellectual property rights of other third parties, which may expose us to litigation and potential liability;

- if one of our third parties is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and

- relationships may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our relationships do not result in the successful discovery, development and commercialization of products or if a third party terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under any third party agreements we enter into, our development of pitolisant or any future product candidates could be delayed and we may need additional resources. Additionally, if any third party terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

Relationships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of future collaborators. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable third parties on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into relationships or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected.

We expect to rely on third parties to conduct our clinical trials for pitolisant and any future product candidate that we decide to develop. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates on a timely basis or at all.

We will continue to rely upon third parties, including independent investigators, to conduct preclinical studies or clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and study or trial sites, which may result in delays to our development timelines and increased costs.

We will have to rely heavily on third parties over the course of our preclinical studies and clinical trials and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol and regulatory requirements. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements for clinical trials, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development.

Regulatory authorities enforce these GCP requirements through periodic inspections of study or trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these clinical trials or perform additional clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP or other applicable requirements. In addition, our clinical trials must be conducted with drug products produced under cGMP requirements and may require a large number of patients. Our failure or any failure by these third parties to comply with these regulations, which would delay the regulatory approval or commercialization process. Moreover, our business may be implicated if any of these third parties violates federal or state laws or regulations including fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any parties conducting our future clinical trials, if any, generally will not be our employees and, except for remedies that may be available to us under our agreements with the third parties conducting such clinical trials, if any, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our current and future product candidates. As a result, our financial results and the commercial prospects for our current and future product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into contractual and other arrangements with alternative CROs or other third parties in a timely manner to meet projected clinical development deadlines or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially affect our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If we experience delays in meeting or fail to meet the regulatory requirements for commercialization of our current or future potential product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We rely completely on third parties to manufacture and distribute our supply of WAKIX, including certain sole-source suppliers and manufacturers, and intend to rely on third parties to manufacture and distribute any future product candidates.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to manufacture or distribute commercial quantities of WAKIX. Our ability to commercially supply WAKIX depends, in part, on the ability of third-party manufacturers to supply and manufacture the raw materials, API and other important components related to the manufacture of WAKIX. We also rely on third parties to package the finished product. These third-party manufacturers have limited experience manufacturing the raw materials and API for WAKIX to be supplied to patients in the United States. Prior to the approval of WAKIX, we experienced minor issues related to product specifications and other minor delays in supply related to our third-party suppliers and manufacturers. While we continue to work with our third-party suppliers and manufacturers to optimize the manufacturing process for WAKIX and will work to optimize the manufacturing process for any future product candidates, we cannot guarantee that even minor changes in the process will result in products that are safe and, where applicable, effective. If we fail to develop and maintain supply relationships with these third parties, we may be unable to continue to successfully commercialize WAKIX.

We rely and will continue to rely on certain third parties as the sole source of the materials they supply or the finished products they manufacture. For example, we rely on Interor S.A., Corden Pharma Chenôve SAS and Patheon UK Limited to provide intermediate supply ingredients, API and finished products, respectively.

Additionally, we rely on our suppliers and manufacturers to purchase materials from other third parties. Any of our existing suppliers or manufacturers may:

- fail to supply us with product on a timely basis or in the requested amount due to unexpected damage to or destruction of facilities or equipment or otherwise;
- fail to increase manufacturing capacity and produce drug product and components in larger quantities and at higher yields in a timely or cost-effective manner, or at all, to sufficiently meet our commercial needs;
- be unable to meet our production demands due to issues related to their reliance on sole- source suppliers and manufacturers;
- supply us with product that fails to meet regulatory requirements;
- become unavailable through business interruption or financial insolvency;
- lose regulatory status as an approved source;
- be unable or unwilling to (i) honor current supply agreements or (ii) renew current supply agreements when such agreements expire on a timely basis, on acceptable terms or at all; or
- discontinue production or manufacturing of necessary drug substances or products.

In the event of any of the foregoing, if we do not have an alternative supplier or manufacturer in place, we would be required to expend substantial management time and expense to identify, qualify and transfer technical processes to alternative suppliers or manufacturers. Transferring technology to other sites may require additional processes, technologies and validation studies, which are costly, may take considerable amounts of time, may not be successful and, in most cases, require review and approval by the FDA. Any need to find and qualify new suppliers or manufacturers could significantly delay production of WAKIX, adversely impact our ability to market WAKIX and adversely affect our business. There can be no assurance that replacements would be available to us on a timely basis, on acceptable terms or at all. Additionally, we and our manufacturers do not currently maintain significant inventory of drug substances and other materials beyond our currently forecasted needs. Any interruption in the supply of a drug substance or other material or in the manufacture of WAKIX could have a material adverse effect on our business, financial condition, operating results and prospects.

Additionally, although we are ultimately responsible for ensuring compliance with regulatory requirements such as cGMPs, we are dependent on our contract suppliers and manufacturers for day-to-day compliance with cGMP for production of both drug substances and finished products. Facilities used by our contract suppliers and manufacturers to produce the drug substances and materials or finished products for commercial sale must pass inspection and be approved by the FDA and other relevant regulatory authorities. A number of our contract suppliers and manufacturers must comply with cGMP requirements enforced by the FDA through its facilities inspection program and review of submitted technical information. If the safety of WAKIX is compromised due to a failure to adhere to applicable laws or for other reasons, we may not be able to successfully commercialize our product and we may be held liable for injuries sustained as a result. In addition, the manufacturing facilities of certain of our suppliers are located outside of the United States. This may give rise to difficulties in importing our product into the United States or other countries as a result of, among other things, regulatory agency approval requirements, taxes, tariffs, local import requirements such as import duties or inspections, incomplete or inaccurate import documentation or defective packaging.

Any of these factors could adversely impact our ability to effectively commercialize WAKIX.

Because a number of companies compete with us, many of which have greater resources than we do, and because we face rapid changes in science in our industry, we cannot be certain that our products will be accepted in the marketplace or capture market share.

Competition from other biotechnology and pharmaceutical companies is intense and is expected to increase. There may be a number of companies pursuing the development of pharmaceuticals in rare neurological disorders, our area of focus. These companies may be very large, and may have financial, technical, sales and distribution and other resources substantially greater than ours. The greater resources of these competitors may enable them to develop, obtain regulatory approval for or market competing products

more quickly or effectively, making it extremely difficult for us to capture a share of the market for our product. We also face competition, and may in the future face additional competition, from manufacturers of generic drugs. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. Generic competition often results in decreases in the prices at which branded products can be sold. The commercial potential of our current products and any future products may be reduced or eliminated if our competitors develop or acquire and commercialize generic or branded products that are safer or more effective, have fewer side effects, are easier to administer or are less expensive than our products. We also face competition from off-label uses of approved drugs. Additionally, the biotechnology and pharmaceutical industries are subject to rapid changes in science, and our competitors may develop and market products with improved therapeutic profiles relative to pitolisant or any future product candidates that would render pitolisant or any future product candidates noncompetitive.

We may need to increase the size and capabilities of our organization based on business need, and we may experience difficulties in managing our growth.

We commenced operations in 2017 and, as of December 31, 2020, had approximately 150 employees. As we advance the development of pitolisant in other indications and commercialize WAKIX as a treatment for EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, we must continue to grow the size of the organization. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining and motivating additional employees;
- effectively managing our development efforts, including the clinical development and FDA or other regulatory authority review processes for pitolisant or any future product candidates;
- effectively managing any third-party service providers involved in the development and manufacture of pitolisant or any future product candidates; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and commercialize WAKIX or any future product candidates will depend, in part, on our ability to effectively manage any future growth. Our management will have to dedicate a significant amount of its attention to managing these growth activities. In addition, we expect to incur additional costs in hiring, training and retaining such additional personnel.

If we are not able to effectively expand our organization, we may not be able to successfully execute the tasks necessary to further develop and commercialize pitolisant or any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our future success depends on our ability to retain our key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

To encourage valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity award grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by changes in the price of our common stock that are beyond our control, and may at any time be insufficient to retain employees who receive more lucrative offers from other companies. Any of our employees could leave our employment at any time, with or without notice.

Recruiting and retaining qualified operations, finance and accounting, quality and compliance, scientific, clinical, manufacturing and sales and marketing personnel or consultants will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms, given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. If we are unable to attract, retain and motivate qualified and experienced personnel, it could harm our business, results of operations and financial condition. Even if we are successful in attracting and retaining such personnel,

competition for such employees may significantly increase our compensation costs and adversely affect our business, results of operations and financial condition.

The loss of the services of any of our executive officers, key employees or consultants could seriously harm our ability to successfully implement our business strategy. Replacing executive officers, key employees or consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel or consultants on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

We may hire part-time employees or use consultants. As a result, certain of our employees, officers, directors or consultants may not devote all of their time to our business, and may from time to time serve as employees, officers, directors and consultants of other companies.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, the manufacturing facilities of our third-party contract manufacturers or our or their distribution networks, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, or interruptions in the commercialization of WAKIX or our business operations. Natural disasters could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities, the manufacturing facilities of our third-party contract manufacturers or our or their distribution networks, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure our investors that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities or the manufacturing facilities of our third-party contract manufacturers are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

We depend on our information technology systems, and any failure of these systems could harm our business. Any real or perceived security breaches, loss of data, and other disruptions or incidents could compromise the privacy, security, integrity or confidentiality of sensitive information related to our business or prevent us from accessing critical information and expose us to liability and reputational harm, which could adversely affect our business, results of operations and financial condition.

We collect and maintain data and information that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business, including systems infrastructure operated and maintained by our third party suppliers or providers. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the privacy, security, confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems and facilities to prevent an information compromise, and rely on commercially available systems, software, tools and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result, a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future

collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to damage or unauthorized access or use resulting from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, denial-of-service attacks, cyber- attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, attachments to emails, persons inside our organization (including employees or contractors), lost or stolen devices, or persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through social engineering attacks, cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a real or perceived security breach affects our systems (or those of our third party providers or suppliers) or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of or other processing of personally identifiable information or clinical trial data, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss, negative publicity, harm to our reputation, governmental investigation and/or enforcement actions, claims or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition. The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we begin to operate in foreign jurisdictions.

Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U.S. federal and state healthcare fraud and abuse laws, data privacy and security laws and other similar non-U.S. laws; or laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use or misrepresentation of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to

detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Development, Regulatory Approval and Commercialization

The regulatory approval process of the FDA is costly, lengthy and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for pitolisant in other potential indications for which we may seek to develop pitolisant, our business will be substantially harmed.

Although the commercialization of WAKIX is our primary focus, as part of our longer-term growth strategy, we plan to evaluate pitolisant in other indications and develop other product candidates. The research, testing, manufacturing, labeling, approval, selling, import, export, pricing and reimbursement marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory agencies in the United States. Although we have obtained regulatory approval for WAKIX in the United States for the treatment of EDS or cataplexy in adult patients with narcolepsy, it is possible that we may not obtain regulatory approval for pitolisant for other indications, or for any other product candidates we may seek to develop in the future. We received a Complete Response Letter for pitolisant for the treatment of cataplexy in adult patients with narcolepsy, and therefore the FDA did not approve WAKIX for this indication during the initial NDA review. Subsequently, in June 2020, we received a general advice letter from the FDA stating that the FDA had re-analyzed data from the HARMONY 1 trial that we submitted in the NDA in support of the adult cataplexy indication for WAKIX. As a result, the FDA recommended we submit a complete response resubmission in pursuit of the adult cataplexy indication for WAKIX. Following such resubmission, we received acknowledgement from the FDA that it considers the resubmission to be a complete Class 1 response to its August 14, 2019 action letter, and the user fee goal date, or decision date, was October 13, 2020. On October 13, 2020 we received regulatory approval for WAKIX for the treatment of cataplexy in adult patients with narcolepsy. Nevertheless, obtaining regulatory approval of an NDA can be a lengthy, expensive and uncertain process.

The FDA can delay, limit or deny approval of a drug candidate for many reasons or require us to conduct additional preclinical or clinical testing, including, but not limited to, the following:

- a drug candidate may not be deemed safe or effective, or the clinical and other benefits may be deemed to not outweigh the candidate's risks;
- the FDA might not approve our trial design and analysis plan;
- the FDA may not find the data from nonclinical and clinical studies and trials sufficient or may disagree with our interpretation of data from nonclinical or clinical studies;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates, or other products containing the active ingredient in our product candidates;
- clinical inspection(s) by the FDA or other regulatory authorities may result in unacceptable findings that could negatively impact approval of pitolisant;
- the FDA might not accept or deem acceptable a third-party manufacturers' processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

Prior to obtaining approval to commercialize a drug candidate in the United States, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, that such drug candidates are safe and effective for their intended uses. The number of nonclinical and clinical studies and trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. In addition, data obtained from preclinical trials and clinical trials are susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials or marketing approval. Furthermore, as more competing drug candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. If pitolisant fails to demonstrate safety and efficacy in clinical trials or does not gain regulatory approval for other indications, our business and results of operations will be materially and adversely harmed. Additionally, if the FDA requires that we conduct additional clinical trials, places limitations on pitolisant in our label, delays approval to market pitolisant or limits the use of pitolisant, our business and results of operations may be harmed.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If we fail to obtain and sustain an adequate level of coverage and reimbursement for WAKIX and other product candidates by third-party payors, sales would be adversely affected.

Successful sales of WAKIX and any other product candidates that may receive regulatory approval depend on the availability of coverage and adequate reimbursement from third-party payors. Patients who are prescribed medications for the treatment of their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their prescription drugs. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Regulatory approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. Commercial third-party payors, such as private health insurers and health maintenance organizations, also decide which medications they will pay for and establish reimbursement levels, though commercial third-party payors often follow CMS' reimbursement determinations. The availability of coverage and the extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of WAKIX or other product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and

- neither experimental nor investigational.

We cannot be sure that reimbursement will be available for WAKIX and, if coverage and reimbursement are available, what the level of reimbursement will be. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Obtaining coverage and reimbursement approval for a product from a government or other third- party payor can be an expensive and time-consuming process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. The industry competition to be included in third-party payors' drug formularies, or lists of medications for which third- party payors provide coverage and reimbursement, often leads to downward pricing pressures on pharmaceutical products. In addition, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access through formulary controls or otherwise to a branded drug when a less costly generic equivalent or other alternative is available. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average manufacture price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level ofreimbursement.

In addition, there may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses.

Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of product from countries where they may be sold at lower prices than in the United States.

While we have obtained coverage for WAKIX from certain third-party payors, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use WAKIX unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of WAKIX. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available. We may suffer loss of corporate reputation due to industry-wide legislative or public scrutiny of our pricing decisions and practices within an increasingly price-sensitive environment.

Despite obtaining formulary approval from certain third-party payors, sometimes with prior authorization or other formulary restrictions and requirements, including documented failure or inadequate response to alternative treatments, we expect to experience pricing pressures in connection with the sale of WAKIX due to the trend toward cost containment, managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. Large public and private payors, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, are questioning the coverage of, and challenging the prices charged for medical products and services, and many third- party payors limit coverage of, or reimbursement for, newly approved health care products. The downward pressure on healthcare costs in general, particularly prescription medicines, medical

devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the successful commercialization of new products. Further, the adoption and implementation of any future governmental cost containment or other health reform initiative may result in additional downward pressure on the price that we may receive for WAKIX.

These cost-control initiatives could decrease the price we have established for WAKIX, which could result in product revenues being lower than anticipated. The pricing, coverage and reimbursement of WAKIX must be adequate to support a commercial infrastructure. If the price for WAKIX decreases or if governmental and other third-party payors do not provide adequate coverage and reimbursement levels, our revenue, gross margins and prospects for profitability will suffer.

While we have not taken any steps to attain regulatory or patent approvals in any specific markets outside of the United States, we plan to explore obtaining additional licensing rights from Bioprojet to expand into international markets with WAKIX**.** Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries will likely put pressure on the pricing and usage of medical products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for WAKIX. Accordingly, in markets outside the United States, the reimbursement for WAKIX may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

WAKIX has been approved by the FDA for the treatment of EDS in adult patients with narcolepsy, and cataplexy in adult patients with narcolepsy. Regulatory approval is limited by the FDA to the specific indication for which approval has been granted and, unless we seek regulatory approval for additional indications, we will be prohibited from marketing pitolisant for other indications. We may be subject to fines, penalties or injunctions if we are determined to have promoted or be promoting the use of pitolisant for unapproved or "off-label" uses, resulting in damage to our reputation and business.

While we received approval for the indications of the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy, WAKIX is not indicated to treat any other conditions. We are prohibited from promoting WAKIX for any other indication unless we are granted FDA approval for such indication. The FDA strictly regulates the promotional claims that may be made about prescription products, and WAKIX may not be promoted for uses that are not approved by the FDA as reflected in its approved labeling. If we are not able to obtain FDA approval for any desired future indications for our products and product candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications that are not specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biotechnology or pharmaceutical companies on off-label use. If the FDA determines that our promotional activities constitute promotion of an off-label use, it could request that we modify our promotional materials and subject us to FDA regulatory or enforcement actions as well as actions by other agencies, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, mandatory or voluntary recalls, civil fines, disgorgement of money, operating restrictions, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement, injunctions or criminal prosecution, any of which could significantly harm our business.

WAKIX or any of our future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, reduce the commercial attractiveness of a prescribing label or result in significant negative consequences following regulatory approval, if approved.

Clinical trials of WAKIX or other product candidates we may develop could reveal a high and unacceptable incidence and severity of undesirable side effects. Undesirable side effects could adversely affect patient enrollment in clinical studies, cause us or regulatory authorities to interrupt, delay or halt clinical studies

or result in the delay, denial or withdrawal of regulatory approval by the FDA or other regulatory authorities. Undesirable or adverse side effects also could result in regulatory authorities mandating a more restrictive prescribing label for the product, which, in turn, could limit the market acceptance of the product even if approved for marketing and commercialization.

Drug-related side effects could result in potential product liability claims. We believe our product liability insurance coverage is sufficient in light of our clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts or maintain coverage at all to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations, business and financial condition. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, significant negative media attention, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our current product candidate or any future product candidate, product recalls, restrictions on labeling, marketing or promotion, decreased demand for our product candidates, if approved for marketing, and loss of revenue.

Additionally, if we or others later identify undesirable side effects caused by WAKIX, either in the post-marketing setting or in clinical trials in other potential indications for which we develop pitolisant, or in clinical trials for other product candidates, a number of potentially significant negative consequences could result, including but not limited to:

- the delay, prevention or withdrawal of approvals by regulatory authorities;
- the requirement of additional warnings on the prescribing label;
- the requirement of a REMS plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers and/or other elements to assure safe use;
- designation as a controlled substance by the DEA;
- litigation and the potential to be held liable for harm caused to patients; and
- an adverse effect on our reputation.

Any of these events could prevent us from achieving or maintaining market acceptance of pitolisant and could significantly harm our business, results of operations, financial condition and prospects.

We have never commercialized a product candidate prior to WAKIX and we may lack the necessary expertise, personnel and resources to successfully commercialize WAKIX or any other potential product candidates that receive regulatory approval on our own or together with collaborators.

WAKIX is our first commercialized product. Prior to this, our operations had been limited to organizing and staffing our company, business planning, raising capital, acquiring the rights to our product candidates and undertaking preclinical studies and clinical trials of our product candidates. We currently have no in-house manufacturing, distribution or supply capabilities. To achieve commercial success of WAKIX or any other product candidate, if approved, we will have to develop our own manufacturing, distribution and supply capabilities or outsource these activities to a third party.

We are early in our commercialization efforts. Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of ANDAs in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labelling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity ("NCE"). Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug.

While we have received five years of NCE exclusivity for WAKIX, manufacturers may seek to launch generic products following the expiration of the applicable exclusivity period we obtain, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could materially and adversely affect our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

To obtain the requisite regulatory approvals to commercialize any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process and our future clinical trial results may not be successful.

We may experience delays in completing our clinical trials or preclinical studies and initiating or completing additional clinical trials. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize the product candidates we develop, including:

- regulators, IRBs or other reviewing bodies may not authorize us or our investigators to commence a clinical trial, or to conduct or continue a clinical trial at a prospective or specific trial site;

- we may not reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- the number of subjects or patients required for clinical trials of pitolisant in additional indications or any other product candidate may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we may have to amend clinical trial protocols submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which we may be required to resubmit to an IRB and regulatory authorities for re-examination;

- regulators, IRBs or other reviewing bodies may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies, or the supply or quality of pitolisant or any other product candidate or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and

- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Regulators, IRBs of the institutions in which clinical trials are being conducted or data monitoring committees may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Negative or inconclusive results from our ongoing clinical trials of pitolisant for the treatment of narcolepsy, or any other clinical trial or preclinical studies in animals that we conduct, could mandate repeated or additional clinical trials and could result in changes to or delays in clinical trials in other indications. We do not know whether any clinical trials that we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market pitolisant for our initial or potential additional indications, or any other product candidate. If later stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for pitolisant for initial or potential additional indications, or any other product candidate, may be adversely impacted.

Our failure to successfully initiate and complete clinical trials of pitolisant for potential additional indications or any other product candidate and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market pitolisant or any other product candidate would significantly harm our business. Our product candidate development costs will also increase if we experience delays in testing or regulatory approvals and we may be required to obtain additional funds to complete clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of pitolisant or any other product candidate.

In addition, prior to our acquisition of the rights to pitolisant, we had no involvement with or control over the nonclinical or clinical development of pitolisant. Additionally, pursuant to our collaboration agreement with Bioprojet, we will rely on data generated by Bioprojet in connection with seeking regulatory approval of pitolisant in the territories in which we have rights to develop and commercialize pitolisant. We are dependent on Bioprojet having conducted such research and development in accordance with the applicable protocols and legal, regulatory and scientific standards, having accurately reported the results of all clinical trials and other research they conducted prior to our acquisition of the rights to pitolisant, having correctly collected and interpreted the data from these trials and other research, and having supplied us with complete information, data sets and reports required to adequately demonstrate the results reported through the date of our acquisition of these assets. Problems related to predecessors could result in increased costs and delays in the development of pitolisant for additional indications, which could adversely affect our ability to generate any future revenue from sales of pitolisant, if approved for additional indications.

Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, "topline" or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available topline data, and the results and related findings and conclusions are subject to change following completion of the study or a full analyses of all data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, "topline" or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. "Topline" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, "topline" data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our business in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the interim, "topline" or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects or financial condition may be harmed.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials on our current timelines, or at all, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Enrollment in our clinical trials may be slower than we anticipate, leading to delays in our development timelines. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, our ability to recruit clinical trial investigators with the appropriate competencies and experience, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical sites, the eligibility criteria for the trial and the proportion of patients screened that meets those criteria, our ability to obtain and maintain patient consents, and the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Furthermore, any negative results or new safety signals we or third parties may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in our clinical trials. Similarly, negative results reported by our competitors about their drug candidates may negatively affect patient recruitment in our clinical trials. In addition, marketing authorization of competitors in this same class of drugs may impair our ability to enroll patients into our clinical trials, delaying or potentially preventing us from completing recruitment of one or more of our trials. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop pitolisant or any future product candidates, or could render further development impossible. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials, and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance.

Even though the FDA granted orphan drug designation to pitolisant for the treatment of narcolepsy, we may not be able to obtain or maintain orphan drug marketing exclusivity for this product candidate or any other product candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Pitolisant was granted orphan drug designation for the treatment of narcolepsy in 2010. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same indication for that time period. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. The applicable exclusivity period is seven years in the United States. Orphan drug exclusivity in the United States may be unavailable where the indication for which the product candidate is approved is broader than the orphan-designated indication, or is otherwise different from the orphan-designated indication. For example, the FDA granted orphan drug designation for pitolisant for the treatment of narcolepsy. Even if we obtain orphan drug exclusivity for a drug candidate, that exclusivity may not effectively protect the candidate from competition. WAKIX may face additional competition because different drugs with a different active moiety can still be approved for the same condition. Even after an approved drug is granted orphan exclusivity, exclusivity may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition following approval. In addition, the FDA can subsequently approve products with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our product candidates in ways that are difficult to predict.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 ("FDARA"). FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease or condition in order to receive orphan drug exclusivity. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We are subject to ongoing regulatory obligations and continued regulatory review with respect to WAKIX, which will result in significant additional expense. Additionally, WAKIX could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with WAKIX.

WAKIX is subject to extensive and ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, distribution, import, export, record keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMP. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Our regulatory approval for WAKIX for the treatment of EDS or cataplexy in adult patients with narcolepsy, and any other regulatory approvals we may receive for pitolisant or any future product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, which must comply with applicable GCP regulations. We could also be asked to conduct post marketing clinical studies to verify the safety and efficacy of future product candidates in general or in specific patient subsets. For example, as a part of the regulatory approval for WAKIX for the treatment of EDS in adult patients with narcolepsy, we are required to conduct post-marketing studies in women exposed to pitolisant in pregnancy, including a

registry-based observational cohort study to assess maternal, fetal, and infant outcomes of women exposed to pitolisant during pregnancy, and another study of a different design such as a case control study or a retrospective cohort study using electronic medical record data, and a lactation study.

We will also be required to report certain adverse events and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for WAKIX. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote WAKIX for indications or uses for which it does not have FDA approval. The holder of an approved NDA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling or manufacturing process.

If a regulatory agency discovers previously unknown problems with WAKIX, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing, or labeling of a product, the regulatory agency may impose restrictions on the product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning or untitled letters;
- impose civil or criminal penalties, including product seizures and injunctions;
- limit or suspend regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities, on the manufacturing of our products, or on the labeling or marketing of our products; or
- seize or detain products or require a product recall or withdrawal of the products from the market.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from WAKIX or future product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from the sale of WAKIX or future product candidates, our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

The regulatory requirements and policies may change, and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we or any future collaboration partner are not able to maintain regulatory compliance, we or such collaboration partner, as applicable, may face government enforcement action and our business will suffer.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, the results of the 2020 U.S. Presidential election may affect our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these executive actions will be implemented, or whether they will be rescinded or replaced under the Biden Administration. The policies and priorities of the Biden Administration are unknown and may materially impact the regulatory framework governing our products. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to

enforcement action and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

Non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. The laws that affect our current and future operations include, but are not limited to:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, in exchange for, or to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item, or service for which payment may be made, in whole or in part, under any U.S. federal healthcare programs, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal civil and criminal false claims laws, such as the False Claims Act ("FCA"), which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, and prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the U.S. federal government, false, fictitious or fraudulent claims for payment of federal funds, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. For example, pharmaceutical companies have been prosecuted under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;

- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;

- HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;

- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;

- state law equivalents of each of the above federal laws, such as state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and may be broader in scope than their federal equivalents;

- federal transparency requirements detailing interactions with and payments to healthcare providers, such as the federal reporting requirements under the Physician Payments Sunshine Act, which requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the HHS information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals starting January 1, 2022, and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members. Failure to submit required information may result in civil monetary penalties;

- state laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation and other remuneration provided to physicians and other health care providers and other potential referral sources, state laws that require drug manufacturers to file reports relating to pricing information and marketing expenditures, state and local laws requiring the registration of pharmaceutical sales representatives;

- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and

- similar healthcare laws in the European Union and EEA and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our business operations and current and future arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices, including, without limitation, our patient support and financial assistance programs, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil, administrative and criminal penalties, damages, fines, the curtailment or restructuring of our operations, contractual damages, disgorgement, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, the exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to market pitolisant, if approved, and adversely impact our financial results. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources.

Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the applicable regulatory agencies or the courts, and their provisions are open to a variety of interpretations.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, the California Consumer Privacy Act of 2018 (the "CCPA") went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. Further, the California Privacy Rights Act (the "CPRA") recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by HITECH. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who enroll in our patient assistance programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required

to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

In Europe, the GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EU and the United States remains uncertain. For example, in 2016, the EU and United States agreed to a transfer framework for data transferred from the EU to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union. Further, from January 1, 2021, companies have to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. Currently there is a four to six-month grace period agreed in the EU and United Kingdom Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. However, it is not clear whether (and when) an adequacy decision may be granted by the European Commission enabling data transfers from EU member states to the United Kingdom long term without additional measures. These changes may lead to additional costs and increase our overall risk exposure.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. If we or third-party CMOs, CROs or other contractors or consultants fail to comply with applicable federal, state or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage.

Clinical practice guidelines and recommendations published by various organizations could have significant influence on the use of WAKIX.

Professional societies, practice management groups, private health and science foundations and organizations involved in various diseases from time to time may publish guidelines or recommendations to the healthcare and patient communities. The recommendations of these groups or organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Recommendations or guidelines suggesting the reduced use of WAKIX or the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use of WAKIX.

Product candidates we develop in the future may be classified as controlled substances, the making, use, sale, importation, exportation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies.

Product candidates we develop in the future may be classified as controlled substances, which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation, exportation and distribution. Controlled substances are regulated under CSA and regulations of the DEA.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances

considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances.

Various states also independently regulate controlled substances. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs as well. While some states automatically schedule a drug when the DEA does so, in other states there must be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could impair the commercial attractiveness of such product. We or our collaborators must also obtain separate state registrations in order to be able to obtain, handle and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

For any of our products or product candidates classified as controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. There is a risk that DEA regulations may limit the supply of the compounds used in clinical trials for our product candidates, and, in the case of our approved products, the ability to produce and distribute our products in the volume needed to meet commercial demand.

Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, recordkeeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates including controlled substances. The DEA, and some states, conduct periodic inspections of registered establishments that handle controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of their restrictive nature, these regulations could limit commercialization of any of our approved products or product candidates that are classified as controlled substances.

Enacted and future healthcare legislative changes may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and affect the prices we may obtain.

In the United States, the European Union and other some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any products for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the ACA, was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the healthcare industry, and impose additional healthcare policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. Among the provisions of the ACA of importance to the pharmaceutical industry and our potential product candidates are the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program for branded and generic drugs;

- a methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been numerous judicial, executive and legislative challenges to certain aspects of the ACA. The U.S. Supreme Court is currently reviewing the constitutionality of the ACA in its entirety. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. While any proposed measures will require authorization through additional legislation to become effective, the probability of their success is uncertain, particularly in light of the new Presidential administration.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. These reforms could reduce the ultimate demand for our commercial products and product candidates, once approved, or put pressure on our product pricing.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and

cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future product candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate Program. Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we have to report on a monthly and quarterly basis to the CMS, the federal agency that administers the Medicaid Drug Rebate Program. These data include, among other things, the average manufacturer price (“AMP”) and, in the case of innovator products, the best price (“BP”) for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly and/or quarterly AMP and BP data on a timely basis could result in a civil monetary penalty for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the 340B program in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B “ceiling price” for the manufacturer’s covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts “orphan drugs” from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA or other legislation or regulation could affect our 340B ceiling price calculations and negatively impact our results of operations commercializing pitolisant. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would

require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

In order to be eligible to have our products that we successfully commercialize paid for with federal funds under the Medicaid program and purchased by certain federal agencies and grantees, we also have to participate in the U.S. Department of Veterans Affairs ("VA"), Federal Supply Schedule ("FSS") pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price ("FCP") to four federal agencies (VA, U.S. Department of Defense ("DOD"), Public Health Service, and U.S. Coast Guard).

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and antimony laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the United States domestic bribery statute contained in 18 U.S.C. § 201, the United States Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the

ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon closing of this offering and in our operations as a U.S. public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any proprietary name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA reviews proposed product names, considering both the potential for the name to lead to medical errors due to confusion with other product names and whether the proposed name is overly fanciful, misleadingly implies unique effectiveness or composition, or contributes to overstatement of product efficacy, minimization of risk, broadening of product indications or unsubstantiated superiority. If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of our existing trademark applications for such product candidate, and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely, and will continue to rely, on a combination of patents, trademarks and confidentiality agreements with employees, consultants, collaborators, advisors and other third parties to protect the intellectual property related to our current and future product candidates. Our success depends in large part on our licensor's ability to obtain and maintain patent protection in the United States with respect to WAKIX and our ability to obtain and maintain patent protection in the United States and any other relevant foreign jurisdictions with respect to any future product candidates that we develop. We seek to ensure that our current and future licensors obtain appropriate patent protection to all product candidates that we license from them. The patent prosecution process is expensive and time- consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Our patent portfolio comprises three U.S. patents exclusively licensed to us from Bioprojet. One U.S. patent, No. 8,207,197 has claims directed to a polymorph, i.e. a specific crystalline form, of pitolisant and, methods for preparing that polymorph of pitolisant, which is expected to expire in February 2029 without taking into consideration any possible patent term extension. A second U.S. patent, No. 8,486,497, has claims directed to methods of treating excessive daytime sleepiness by administering pitolisant, which is expected to expire in September 2029 without taking into consideration any possible patent term extension. With all applicable patent term adjustments available and granted to us, the term of the last-to-expire pitolisant-related patent in our portfolio extends to September 2029.

The patents that we in-license now or the patents and patent applications that we own or in-license in the future may not have patentable claims that protect our current and future product candidates in the relevant jurisdictions where we intend to commercialize such products. There is no assurance that we and our licensor are aware of all potentially relevant prior art relating to future patent applications. As such, the patent examiner may find prior art that can prevent a patent from issuing from a pending patent application. During the patent examination process, we or our licensor may be required to narrow the pending claims to overcome prior art, a process that may limit the scope of patent protection. Even if patents do successfully issue based on our future patent applications, and even if the issued patents cover our current and future product candidates, including their compositions formulation, method of manufacture, and method of use, third parties may challenge our issued patents' validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us in the future could deprive us of rights necessary for the successful commercialization of any of our current or future product candidates, if approved. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

If the patent applications we may own or in-license in the future with respect to our current and future product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for any of our current or future product candidates, it could dissuade other companies from collaborating with us to develop future product candidates, and threaten our ability to commercialize our current and future product candidates. Notably, pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Any such outcome could have an adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act (the “Leahy-Smith Act”) was signed into law. The Leahy-Smith Act made a number of significant changes to United States patent laws. These include provisions that affect the way patent applications are prosecuted and challenged at the USPTO and may also affect patent litigation. The USPTO has developed and continues to develop new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it remains unclear what impact the Leahy-Smith Act, subsequent rulemaking, and judicial interpretation of the Leahy-Smith Act and regulations will have on the operation of our business. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business and financial condition. Moreover, future changes to the patent laws of the United States and foreign jurisdictions may adversely affect the term, scope, validity and enforceability of our or our licensor’s patent rights. For example, a new bill (Terminating the Extension of Rights Misappropriated Act, or TERM Act, H.R. 3199) percolating through the United States Congress aims to reduce the term of certain drug patents in order to ease generic entry and increase competition.

The inventorship and ownership rights for patents that we in-license or may own or in-license in the future may be challenged by third parties. Such challenges could result in loss of exclusive rights to such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or require us to obtain a license from such third parties on commercially reasonable terms to secure exclusive rights. If any such challenges to inventorship or ownership were asserted, there is no assurance that a court would find in our favor or that, if we choose to seek a license, such license would be available to us on acceptable terms or at all.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in pre- and post-issuance opposition, derivation, re-examination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications, whether owned or in-licensed now or in the future, is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our licensed patents may be challenged in the courts or patent offices in the United States. Such challenges may

result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after the filing of the earliest non-provisional application to which the patent claims priority. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. We may be required to disclaim a portion of patent term in order to overcome double patenting rejections from the patent office, thus potentially shortening our exclusivity period. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our current and future product candidates.

We have licensed certain intellectual property rights covering pitolisant from Bioprojet, and we may license intellectual property rights from others in the future. If, for any reason, our license agreement with Bioprojet or any future licensor is terminated or we otherwise lose the rights associated with a license, it could adversely affect our business. Our license agreement with Bioprojet imposes, and any future collaboration agreements or license agreements we enter into are likely to impose various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. If we breach any material obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology, or having to negotiate new or reinstated licenses on less favorable terms, or enable a competitor to gain access to the licensed technology.

If we do not obtain protection under the Hatch-Waxman Amendments by extending the patent term for our current and future product candidates, our business may be harmed.

Our commercial success will largely depend on our licensor's ability to obtain and maintain patent and other intellectual property in the United States for pitolisant, and our target indications, and our ability to maintain obtain and maintain patent and other intellectual property in the United States for any product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting product candidates might expire before or shortly after such candidates begin to be commercialized. We expect to seek extensions of patent terms in the United States.

Depending upon the timing, duration and specifics of FDA marketing approval of our current and future product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years beyond the normal expiration of the patent as compensation for patent term lost during drug development and the FDA regulatory review process, which is limited to the approved indication (or any additional indications approved during the period of extension). This extension is limited to only one patent that covers the approved product, the approved use of the product, or a method of manufacturing the product. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time-period or the scope of patent protection afforded could be less than we request.

If we or our licensor are unable to extend the expiration date of our or their existing patents or obtain new patents with longer expiry dates, as applicable, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case.

The validity, scope and enforceability of any patents listed in the Orange Book that cover our current and future product candidates can be challenged by third parties.

One or more third parties may challenge the current patents, or future patents within our portfolio, which could result in the invalidation of, or render unenforceable, some or all of the relevant patent claims or a finding of non-infringement. For example, if a third party files an ANDA for a generic drug containing pitolisant, and relies in whole or in part on studies conducted by or for us, the third party will be required to certify to the FDA that either: (1) there is no patent information listed in the FDA's Orange Book with respect to our NDA for the applicable approved product candidate; (2) the patents listed in the Orange Book have expired; (3) the listed patents have not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patents are invalid or will not be infringed by the manufacture, use or sale of the third party's generic drug. A certification that the new drug will not infringe the Orange Book-listed patents for the applicable approved product candidate, or that such patents are invalid, is called a paragraph IV certification. If the third party submits a paragraph IV certification to the FDA, a notice of the paragraph IV certification must also be sent to us once the third party's ANDA is accepted for filing by the FDA. We may then initiate a lawsuit to defend the patents identified in the notice. The filing of a patent infringement lawsuit within 45 days of receipt of the notice automatically prevents the FDA from approving the third party's ANDA until the earliest of 30 months or the date on which the patent expires, the lawsuit is settled, or the court reaches a decision in the infringement lawsuit in favor of the third party. If we do not file a patent infringement lawsuit within the required 45-day period, the third party's ANDA will not be subject to the 30-month stay of FDA approval.

Moreover, a third party may challenge the current patents, or future patents within our portfolio, which could result in the invalidation of some or all of the patents that might otherwise be eligible for listing in the Orange Book for one of our products. If a third party successfully challenges all of the patents that might otherwise be eligible for listing in the Orange Book for one of our products, we will not be entitled to the 30-month stay of FDA approval upon the filing of an ANDA for a generic drug containing, for example, pitolisant, and relies in whole or in part on studies conducted by or for us.

Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be very expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could limit our ability to prevent third parties from competing with our current and future product candidates.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain patents and patent applications, whether owned or in-licensed now or in the future, covering any of our current or future product candidates, our competitors might be able to enter the market, which would have an adverse effect on our business.

We may need to acquire or license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our current and future product candidates. It may be necessary for us to use the patented or proprietary technology of one or more third parties to commercialize our current and future product candidates. If we are unable to acquire such intellectual property outright, or obtain licenses to such intellectual property from such third parties when needed or on commercially reasonable terms, our ability to commercialize our current and future product candidates, if approved, would likely be delayed.

The risks described elsewhere pertaining to our intellectual property rights also apply to the intellectual property rights that we in-license, and any failure by us or our licensors to obtain, maintain, defend and enforce these rights could have an adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and may not have sufficient ability to provide input into the patent prosecution, maintenance and defense process with respect to such patents, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain, defend and enforce the licensed patents.

Third-party claims or litigation alleging infringement of patents or other proprietary rights, or seeking to invalidate patents or other proprietary rights, may delay or prevent the development and commercialization of any of our current or future product candidates.

Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, interferences, derivation and administrative law proceedings, inter partes review and post-grant review before the USPTO, as well as oppositions and similar processes in foreign jurisdictions. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are or may in the future be developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties.

Third parties may assert that we are infringing their patents or employing their proprietary technology without authorization.

There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our current and future product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our current and future product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our current and future product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent was to be held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our current and future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our current and future product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our current and future product candidates, which could harm our business significantly. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our current and future product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our current product candidate in any jurisdiction.

It is possible that we and our current and future licensors will fail to identify patentable aspects of research and development output before it is too late to obtain patent protection. The patent applications that we may own or in-license in the future may fail to result in issued patents with claims that cover our current and future product candidates. We and our current and future licensors may also inadvertently make statements to regulatory agencies during the regulatory approval process that may be inconsistent with positions that have been taken during prosecution of the patent applications, which may result in such patents being narrowed, invalidated or held unenforceable.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively affect our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, and our failure to identify and correctly interpret relevant patents may negatively affect our ability to develop and market our products.

We may become involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate the patents of our licensor or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that an asserted patent is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that the asserted patent does not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of asserted patents at risk of being invalidated or interpreted narrowly and could put a related patent application at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter claims against us such as claims asserting that our patents are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte re-examinations, inter partes review, or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we may license in the future, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to detect or prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on

commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common shares.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our in-licensed patents, any patents that may be issued as a result of our future patent applications, or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our shareholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has recently enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit have issued numerous precedential opinions in recent years narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

The U.S. federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a “nonexclusive, non-transferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees’ former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire

employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self- executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we or our licensors fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we and our licensors are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Any trademarks we have obtained or may obtain may be infringed or be successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our current and future product candidates that are approved for marketing from the products of our competitors. For example, we are marketing pitolisant for the treatment of EDS or cataplexy in adult patients with narcolepsy under the brand name WAKIX, which we have licensed from Bioprojet. We may design or create new trademarks and apply to register them, our trademark applications may not be approved in the United States or any relevant foreign jurisdiction. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks. If we attempt to enforce our trademarks and assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Risks Related to Being a Public Company

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance with our public company responsibilities and corporate governance practices.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002 (the “Sarbanes Oxley Act”), the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel will need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. If, notwithstanding our efforts to comply with new or changing laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us, and our business may be harmed. Further, failure to comply with these laws, regulations and standards may make it more difficult and more expensive for us to obtain directors’ and officers’ liability insurance, which could make it more difficult for us to attract and retain qualified members to serve on our board of directors or committees or as members of senior management. We cannot predict or estimate the amount of additional costs we will incur as a public company or the timing of such costs.

As a result of becoming a public company, we will be obligated to develop and maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common shares.

We will be required, pursuant to Section 404 of the Sarbanes Oxley Act (“Section 404”), to furnish a report by management on, among other things, the effectiveness of our internal controls over financial reporting for the fiscal year beginning January 1, 2022. This assessment will need to include disclosure of any material

weaknesses identified by our management in our internal controls over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting until our first annual report required to be filed with the SEC following the date we are no longer an emerging growth company, as defined in the JOBS Act. At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered public accounting firm. We will be required to disclose significant changes made in our internal controls procedures on a quarterly basis.

We are beginning the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404, and we may not be able to complete our evaluation, testing and any required remediation in a timely fashion. Our compliance with Section 404 will require that we incur substantial legal, accounting and other compliance expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and finance staff and consultants with appropriate public company experience and technical accounting knowledge and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404.

During the evaluation and testing process of our internal controls, if we identify one or more material weaknesses in our internal controls over financial reporting, we will be unable to assert that our internal controls over financial reporting are effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls over financial reporting in the future. Any failure to maintain effective internal controls over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal controls over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal controls over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common shares could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal controls over financial reporting, or to implement or maintain other effective control systems required of public companies, could also negatively impact our ability to access to the capital markets.

In addition, effective disclosure controls and procedures enable us to make timely and accurate disclosure of financial and non-financial information that we are required to disclose. As a public company, if our disclosure controls and procedures are ineffective, we may be unable to report our financial results or make other disclosures accurately on a timely basis, which could cause our reported financial results or other disclosures to be materially misstated and result in the loss of investor confidence and cause the market price of our common shares to decline. If we were to subsequently elect instead to comply with these public company effective dates, such election would be irrevocable pursuant to the JOBS Act.

We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this exemption from new or revised accounting standards and, therefore, we will not be subject to the same new or revised accounting standards as other public companies that have not made this election.

For as long as we continue to be an emerging growth company, we also intend to take advantage of certain other exemptions from various reporting requirements that are applicable to other public companies including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the closing of our IPO; (iii) the date on which we have issued more than $1.0

billion in nonconvertible debt during the previous three fiscal years; or (iv) the date on which we are deemed to be a "large accelerated filer" under the rules of the SEC.

Our management team has limited experience managing a public company.

Our chief executive officer does not have experience managing a public company, interacting with public company investors or complying with the increasingly complex laws pertaining to public companies. Our management team, as a whole, may not successfully or efficiently manage the transition to being a public company subject to significant regulatory oversight and reporting obligations under the federal securities laws and the continuous scrutiny of securities analysts and investors. These new obligations and constituents will require significant attention from our senior management, particularly from our chief executive officer, and could divert their attention away from the day-to-day management of our business, which could adversely affect our revenue, business, results of operations and financial condition.

Risks Related to Ownership of our Common Stock

Our directors, officers and principal stockholders beneficially own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2020, our directors, officers, five percent or greater stockholders, and their respective affiliates beneficially owned in the aggregate approximately 80% of our outstanding voting stock. As a result, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, and approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Future sales of our common stock in the public market, including our directors, officers, or significant shareholders, could cause our share price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Certain holders of our common stock are entitled to rights with respect to registration of such shares under the Securities Act pursuant to a registration rights agreement between such holders and us. If such holders, by exercising their registration rights, sell a large number of shares, they could adversely affect the market price for our common stock. Subject to compliance with applicable securities laws, our officers, directors and other shareholders and their respective affiliates may sell some or all of their common shares in the future. No prediction can be made as to the effect, if any, such future sales will have on the market price of the common shares prevailing from time to time.

If securities or industry analysts do not publish research or publish unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. Moreover, if our operating results do not meet the expectations of the investor community, one or more of the analysts who cover our company may change their recommendations regarding our company, and our stock price could decline.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting pitolisant;

- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;

- the achievement and timing of milestone payments under our existing collaboration and license agreements; and

- the level of underlying demand for WAKIX and customers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

An active trading market for our common stock may not be maintained.

Our common stock only recently began trading on the Nasdaq Global Market, and we can provide no assurance that we will be able to maintain an active trading market on The Nasdaq Global Market or any other exchange in the future. If an active trading market for our common stock is not maintained, or if we fail to satisfy the continued listing standards of The Nasdaq Global Market for any reason and our common stock is delisted, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Future sales and issuances of our common stock or rights to purchase our common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause the stock price of our common stock to decline.

In the future, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. We also expect to issue common stock to employees, consultants and directors pursuant to our equity incentive plans. If we sell common stock, convertible securities or other equity securities in subsequent transactions, or common stock is issued pursuant to equity incentive plans, investors may be materially diluted. New investors in such subsequent transactions could gain rights, preferences and privileges senior to those of holders of our common stock.

We have never paid dividends on our common stock and we do not intend to pay dividends for the foreseeable future. Consequently, any gains from an investment in our common stock will likely depend on whether the price of our common stock increases.

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investments. Furthermore, we are party to a Credit Agreement with OrbiMed that contains negative covenants that limit our ability to pay dividends.

Our charter documents and Delaware law could prevent a takeover that stockholders consider favorable and could also reduce the market price of our stock.

Our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it more difficult for stockholders to elect directors and take other corporate actions. These provisions include:

- providing for a classified board of directors with staggered, three-year terms;

- authorizing our board of directors to issue preferred stock with voting or other rights or preferences that could discourage a takeover attempt or delay changes in control;

- prohibiting cumulative voting in the election of directors;

- providing that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;

- prohibiting the adoption, amendment or repeal of our amended and restated bylaws or the repeal of the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors without the required approval of at least 66.67% of the shares entitled to vote at an election of directors;

- prohibiting stockholder action by written consent;

- limiting the persons who may call special meetings of stockholders; and

- requiring advance notification of stockholder nominations and proposals.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

In addition, we are subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law (the "DGCL"). Under Section 203 of the DGCL, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

These and other provisions in our amended and restated certificate of incorporation and our amended and restated bylaws and under Delaware law could discourage potential takeover attempts, reduce the price investors might be willing to pay in the future for shares of our common stock and result in the market price of our common stock being lower than it would be without these provisions.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;

- any action asserting a claim of breach of a fiduciary duty owed by, or other wrongdoing by, any of our current or former directors, officers, employees or our stockholders;

- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws (as either may be amended from time to time) or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; and

- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our stockholders are deemed to have notice of and have consented to the provisions of our amended and restated certificate of incorporation related to choice of forum. This exclusive forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find the exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;

- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;

- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;

- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;

- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and

- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We do not own any real property. Our corporate headquarters are located in Plymouth Meeting, Pennsylvania. In December 2020, we leased additional office space at this same location, which increased our footprint to approximately 28,638 square feet of space pursuant to a lease that expires in 2024. We believe that our facilities are suitable to meet our current needs.

Item 3. Legal Proceedings.

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. The results of any current or future litigation cannot be predicted with certainty, and regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We do not believe that we have any pending litigation that, individually or in the aggregate, would have a material adverse effect on our results of operations, financial condition or cash flows.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock began trading on the Nasdaq Global Market under the symbol "HRMY" on August 19, 2020. Prior to that date, there was no public trading market for our common stock.

Holders

As of March 15, 2021, we had 53 holders of record of our common stock. Because many of our shares of common stock are held by brokers and other institutions on behalf of shareholders, we are unable to estimate the total number of beneficial owners of our common stock represented by these holders.

Dividend Policy

We currently intend to retain all available funds and any future earnings to fund the development and growth of our business and to repay future indebtedness, if any, and therefore we do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. Any future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to compliance with contractual restrictions and covenants in the agreements governing our current and future indebtedness. Any such determination will also depend upon our business prospects, results of operations, financial condition, cash requirements and availability, industry trends and other factors that our board of directors may deem relevant.

IPO Summary

On August 21, 2020, we completed the IPO of our common stock, in which we issued and sold 6,151,162 shares, including 802,325 shares pursuant to the underwriters' over-allotment option at a price of $24.00 per share for an aggregate price of approximately $147.6 million. The shares began trading on the Nasdaq Global Market on August 19, 2020. The offer and sale of the shares in our IPO was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-240122), which was declared effective by the SEC on August 18, 2020 (the "Registration Statement"). The offering commenced on August 6, 2020 and terminated after the sale of all securities registered pursuant to the Registration Statement. Goldman Sachs & Co. LLC, Jefferies LLC and Piper Sandler & Co. acted as managing underwriters for the offering. We raised approximately $135.4 million, after deducting underwriting discounts and commissions and offering expenses of approximately $12.2 million. None of these expenses consisted of direct or indirect payments made by us to (i) our directors, officers or their associates, (ii) persons owning 10% or more of our common stock or (iii) to our affiliates. There has been no material change in the planned use of proceeds from our IPO as described in the Prospectus. Net proceeds from our IPO have been invested in short-term, interest-bearing, investment grade securities.

Recent Sales of Unregistered Securities

Between January 1, 2020 and August 17, 2020, we issued to certain employees and directors an aggregate of 21,836 shares of our common stock upon the exercise of options issued under the 2017 Equity Plan at an exercise price of $8.22 per share, for an aggregate exercise price of $0.2 million.

Unless otherwise stated, the sales of the above securities were deemed to be exempt from registration under the Securities Act in reliance upon Section 4(a)(2) of the Securities Act (or Regulation D or Regulation S promulgated thereunder), or Rule 701 promulgated under Section 3(b) of the Securities Act as transactions by an issuer not involving any public offering or pursuant to benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of the securities in each of these transactions represented their intentions to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were placed upon the stock certificates issued in these transactions.

Item 6. Selected Financial Data.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes included elsewhere in this Annual Report. This discussion contains forward-looking statements based upon current plans, expectations and beliefs involving risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" and in other parts of this Annual Report.

Overview

We are a commercial-stage pharmaceutical company focused on developing and commercializing innovative therapies for patients living with rare neurological disorders who have unmet medical needs. Our product, WAKIX (pitolisant), is a first-in-class molecule with a novel mechanism of action ("MOA") specifically designed to increase histamine signaling in the brain by binding to H_3 receptors. In August 2019, WAKIX was approved by the U.S. Food and Drug Administration (the "FDA") for the treatment of excessive daytime sleepiness ("EDS") in adult patients with narcolepsy, and its U.S. commercial launch was initiated in November 2019. On October 13, 2020, WAKIX was approved by the FDA for the treatment of cataplexy in adult patients with narcolepsy. WAKIX is the first-and-only approved product for patients with narcolepsy that is not scheduled as a controlled substance by the Drug Enforcement Administration (the "DEA").

We plan to pursue label expansion for WAKIX in narcolepsy in pediatric patients and engage with the FDA in pursuit of pediatric exclusivity. We currently expect to initiate a Phase 3 clinical trial in pediatric patients in the second half of 2021 in pursuit of indications for both EDS and cataplexy. We believe that pitolisant's ability to regulate histamine gives it the potential to provide therapeutic benefit in other rare neurological disorders that are mediated through H_3 receptors and histamine signaling. We are initially focusing on the treatment of EDS associated with Prader-Willi Syndrome ("PWS") and myotonic dystrophy, otherwise known as dystrophia myotonica ("DM"). In December 2020, we initiated a Phase 2 clinical trial to evaluate pitolisant for the treatment of EDS and other key symptoms in patients with PWS and anticipate topline results in the first half of 2022. We are also planning to commence a Phase 2 clinical trial in adult patients with DM in the first half of 2021, with topline results expected in the second half of 2022, under our open Investigational New Drug application ("IND"). Beyond these indications, we intend to further explore pitolisant in other rare neurological disorders in which fatigue and cognitive impairment are prominent symptoms with significant impact on daily functioning.

We also seek to expand our pipeline through the acquisition of additional assets that focus on addressing the unmet needs of patients with neurological disorders. We intend to target assets that will be complementary to WAKIX and our expanding list of potential new indications for WAKIX, and assets that will allow us to further leverage the expertise and infrastructure that we have successfully built at Harmony.

Pitolisant was developed by Bioprojet and approved by the European Medicines Agency ("EMA") in 2016 for the treatment of narcolepsy in adult patients with or without cataplexy. We acquired an exclusive license to develop, manufacture and commercialize pitolisant in the United States pursuant to our license agreement with Bioprojet (as amended, the "Bioprojet License Agreement") in July 2017. See "Part I—Item 1. Business.—Strategic Agreement—License and Commercialization Agreement with Bioprojet" for further information regarding the Bioprojet License Agreement. Pitolisant was granted Orphan Drug Designation for the treatment of narcolepsy by the FDA in 2010. It received Breakthrough Therapy designation for the treatment of cataplexy in patients with narcolepsy and Fast Track status for the treatment of EDS and cataplexy in patients with narcolepsy in April 2018.

Our operating subsidiary, Harmony Biosciences, LLC, was formed in May 2017. We were formed in July 2017 as Harmony Biosciences II, LLC, a Delaware limited liability company, and we converted to a Delaware corporation named Harmony Biosciences II, Inc. in September 2017. In February 2020, we changed our name to Harmony Biosciences Holdings, Inc. Our operations to date have consisted of building and staffing our organization, acquiring the rights to pitolisant, raising capital, opening an IND for pitolisant, initiating an Expanded Access Program ("EAP") for pitolisant for appropriate patients in the United States, preparing and submitting our NDA for pitolisant, gaining NDA approval for WAKIX for the treatment of EDS or cataplexy in adult patients with narcolepsy, and launching and commercializing WAKIX in the United States. In addition, we have initiated or intend to initiate clinical development programs in PWS, DM and pediatric narcolepsy to pursue potential new indications.

Initial Public Offering

On August 21, 2020, we completed the initial public offering ("IPO") of our common stock, in which we sold 6,151,162 shares, including 802,325 shares pursuant to the underwriters' over-allotment option. The shares began trading on the Nasdaq Global Market on August 19, 2020. The shares were sold at an IPO price of $24.00 per share for net proceeds of approximately $135.4 million, after deducting underwriting discounts and commissions and offering expenses of approximately $12.2 million. Upon the closing of the IPO, all outstanding shares of our convertible preferred stock were automatically converted into shares of common stock and the accrued dividend payable to holders of the convertible preferred stock was paid out in shares of common stock, resulting in a total of 42,926,630 shares of common stock being issued to former holders of our convertible preferred stock, and warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for a total of 410,239 shares of common stock.

Liquidity and Sources of Funding

For the year ended December 31, 2020, we generated $159.7 million of net product revenues. We have financed our operations primarily with (a) proceeds from sales of our convertible preferred stock, (b) borrowings under (i) our multi-draw term loan agreement (the "Loan Agreement") with CRG Servicing LLC ("CRG") and (ii) our credit agreement (the "Credit Agreement") with OrbiMed Royalty & Credit Opportunities III, LP ("OrbiMed"), and (c) proceeds from our IPO. As of December 31, 2020, we had cash, cash equivalents and restricted cash of $229.4 million and accumulated deficit of $488.2 million. As of December 31, 2020, we had outstanding debt, net of issuance costs, of $194.3 million.

We believe that our anticipated cash from operating and financing activities and existing cash and cash equivalents will enable us to meet our operational liquidity needs and fund planned investing activities for the next twelve months. We have based this estimate on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Our revenues and expenses in future quarters may differ from our expectations as we:

- commercialize WAKIX in the United States for the treatment of EDS or cataplexy in adult patients with narcolepsy;
- incur sales and marketing costs to support the commercialization of WAKIX and any additional product candidates;
- pay royalties and make milestone payments to Bioprojet for the license of WAKIX;
- incur manufacturing costs for WAKIX and any additional product candidates;
- implement post-approval requirements related to WAKIX;
- conduct clinical trials in PWS, DM, and potential new indications for pitolisant or any additional product candidates;
- conduct a pediatric narcolepsy program in pursuit of an indication and extension of our patents based on pediatric exclusivity;
- conduct earlier stage research and development activities for pitolisant;
- support independent investigator-initiated research for which there is a valid scientific rationale;
- hire additional personnel;
- invest in measures to protect and expand our intellectual property;
- incur interest expenses in conjunction with our debt facility;
- seek regulatory approvals for pitolisant or any additional product candidates that successfully complete clinical development;

- conduct additional clinical trials in pursuit of potential new indications for pitolisant; acquire or in-license other assets and technologies; and

- incur additional costs associated with being a public company.

Commercial Launch Metrics

As of December 31, 2020, over 2,400 unique healthcare professionals ("HCPs") (out of a total of approximately 8,000 HCPs who treat approximately 90% of diagnosed narcolepsy patients) have prescribed WAKIX since it became available in November 2019. The average number of patients on WAKIX at the end of 2020 was approximately 2,500. We have secured formulary access for approximately 80% of all insured lives (Commercial, Medicare and Medicaid) in the United States. Within these covered lives, we have observed favorable access to WAKIX subsequent to the expanded approval of WAKIX for the treatment of cataplexy in adult patients with narcolepsy in October 2020.

COVID-19 Business Update

With the global impact of the COVID-19 pandemic, we have developed a response strategy that includes establishing cross-functional response teams and implementing business continuity plans to manage the impact of the pandemic on our employees, patients, HCPs, and our business.

Despite our response strategy, the COVID-19 pandemic is having an effect on our business and the pharmaceutical industry in general, and is impacting the way stakeholders interact with one another during this pandemic. We continue to leverage technology and virtual engagement initiatives to offset our reduced in-person access to HCPs. The COVID-19 pandemic, which has led to high unemployment and corresponding loss of medical insurance, has caused a change in relationship dynamics between patients and their HCPs and has impacted the way patients take, or do not take, their medication. Based on these factors, we expect that the revenue growth rate in possible future quarters may be adversely impacted by the ongoing COVID-19 pandemic.

We continue to identify new and innovative ways to maintain meaningful engagement, generate awareness and educate our patients, HCPs and payors to minimize the pressure from the COVID-19 pandemic on our business and support our commercial launch performance.

Commercialization

With respect to our commercialization activities, we believe the COVID-19 pandemic is putting pressure on top-line prescription demand for WAKIX, primarily due to (i) our field sales team's reduced ability to access HCPs in person, and (ii) fewer patients seeing HCPs for prescriptions or treatments. The impact on demand for WAKIX may also be related to a reduced ability of prescribers to diagnose narcolepsy patients given the limitations in access to sleep testing, the reduced ability to see patients due to (i) cancelled appointments and (ii) the reprioritization of healthcare resources toward the treatment of COVID-19, both of which lead to fewer prescriptions. Despite these challenges, we continue to engage and educate HCPs virtually on the overall benefit/risk profile of WAKIX and continue to provide support for people living with narcolepsy. As offices, clinics and institutions have begun to allow limited in-person interactions pursuant to health authority and local government guidelines, our field teams continue to re-initiate in-person interactions with HCPs and customers, but the timing and level of engagement vary by account and region and may be adversely impacted in the future where reemergence or future outbreaks of COVID-19 may occur.

High unemployment and the corresponding loss of health insurance is causing some eligible patients to shift from commercial insurance to free goods and patient assistance programs, which impacts our ability to convert demand to revenue. Depending on the scale and ultimate duration of the COVID-19 pandemic and the extent of an economic slowdown, widespread unemployment and resulting loss of employer-sponsored insurance coverage, we may experience a shift from commercial payor coverage to government payor coverage or continued/increased demand for patient assistance and/or free drug programs, which could further impact our net revenue in the coming quarters.

Supply Chain

We currently expect to have adequate supply of WAKIX through the first half of 2022, with additional API on-hand inventory to support 12 to 18 months beyond this time frame. We are working closely with our third-party manufacturers, distributors and other partners to manage our supply chain activities and mitigate potential disruptions to our product supplies as a result of the COVID-19 pandemic. We believe that our access to the required production lines to produce additional API and WAKIX finished product throughout the next 12-18 months will not be directly impacted by the potential need to reprioritize manufacturing resources due to the production of materials utilized for COVID-19 vaccines.

Our manufacturing partners in France and the United States continue to be operational. If the COVID-19 pandemic persists for an extended period of time and/or begins to impact essential distribution systems such as transatlantic freight, FedEx, UPS and postal delivery, we could experience disruptions to our supply chain and operations with associated delays in the manufacturing and supply of our products.

Research and Development

The COVID-19 pandemic has negatively impacted the pharmaceutical industry's ability to conduct clinical trials. While we initially experienced some challenges due to the COVID-19 pandemic, we have taken measures and put contingency plans in place in order to advance our clinical development programs. We have implemented remote and virtual approaches to clinical trials, including using telemedicine for remote clinic visits to perform efficacy assessments and sending out licensed HCPs to each patient to collect safety assessments (e.g. labs, electrocardiograms) as required by the protocols. We are also performing remote site visits and data monitoring where possible. These measures are being instituted with the intent of maintaining patient safety and trial continuity while preserving study integrity. One unique challenge we are facing is the ability to access sleep labs during the COVID-19 pandemic in order to conduct objective sleep testing, which is required for some of our clinical trials. In addition, we rely on contract research organizations ("CROs") or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. If the COVID-19 pandemic continues and persists for an extended period of time, or reemerges in the future, we could experience significant delays in our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Corporate Development and Other Financial Impacts

The COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of domestic and global financial markets. If the disruption persists and/or worsens, we may be unable to access additional capital, which could negatively affect our ability to execute on certain corporate development transactions or other important investment opportunities. The pandemic could also impact our ability to conduct in-person due diligence, negotiations, and other interactions to identify new opportunities.

The COVID-19 pandemic has also affected, and continues to affect, our business operations and financial results. The extent of the impact of the COVID-19 pandemic on our ability to generate sales of, and revenues from, our approved products, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of or reemergence of outbreaks, governmental travel restrictions, quarantines, social distancing and business closure requirements in the United States, France, and other countries, and the effectiveness of actions taken globally to contain and treat COVID-19.

Corporate Responsibility Impact

We continue to provide support to our local communities, patient-focused organizations and other charitable organizations during the COVID-19 pandemic with relief efforts, including corporate donations, supplying food, medical supplies and other resources. For the safety and well-being of our employees, consultants and their families, during the COVID-19 pandemic, we have abided by the government issued work from home orders. We continue to clean and sanitize our offices on a regular basis and have implemented COVID-19 screening procedures and social distancing guidelines before allowing employees or guests to enter our offices.

Financial Operations Overview

Revenue

We did not generate any revenue from inception until the fourth quarter of 2019. Our current product, WAKIX, was approved by the FDA for the treatment of EDS in adult patients with narcolepsy in August 2019, became commercially available in November 2019 and was approved by the FDA for the treatment of cataplexy in adult patients with narcolepsy in October 2020. For the years ended December 31, 2020 and 2019, we had $159.7 million and $6.0 million, respectively, of net product revenue.

Total revenue consists of net sales of WAKIX. Net sales represent the gross sales of WAKIX less provisions for product sales discounts and allowances. At this time, these provisions include trade allowances, rebates to government and commercial entities, and discounts. Although we expect net sales to increase over time, the provisions for product sales discounts and allowances may fluctuate based on the mix of sales to different customer segments and/or changes in our accrual estimates. For further discussion of the components of Revenue, see "—Critical Accounting Policies and Significant Judgments and Estimates."

Cost of Product Sales

Cost of product sales includes manufacturing and distribution costs, the cost of the drug substance, FDA program fees, royalties due to third parties on net product sales, freight, shipping, handling, storage costs and salaries of employees involved with production. We began capitalizing inventory upon FDA approval of WAKIX. A portion of the inventory sold during the year ended December 31, 2020 was produced prior to FDA approval and, therefore, expensed previously as research and development expense in 2019 in the amount of $1.3 million. Excluded from cost of product sold is amortization of acquired developed technology of $9.8 million and $2.8 million in the years ended December 31, 2020 and 2019, respectively.

Previously expensed inventory that was manufactured in anticipation for commercialization preapproval has not had a material impact on our historical results of operations and is not expected to have a material impact on future results of operations. Further, previously expensed inventory has not had a material impact on our gross margin percentage historically, and we do not anticipate a material impact on our gross margin percentage once our previously expensed inventories have been exhausted. Our cost of product sales is increasing moderately as we continue to ramp up production and sales infrastructure to meet expected demand for WAKIX.

The shelf life of our product is three years from date of manufacture, with the earliest expiration of current inventory expected to be May 2022. As of December 31, 2020, we expect our existing inventory to have minimal obsolescence. We will continue to assess obsolescence in future periods as demand for WAKIX and the rate of inventory turnover evolves.

Research and Development Expenses

Our research and development expenses have primarily been limited to the license of the rights to pitolisant, the establishment of an EAP to provide appropriate patients with pitolisant at no cost as part of a clinical trial to assess safety prior to the approval of WAKIX, the preparation of the NDA, and the initiation of a development program for new indications for pitolisant in patients with PWS, DM and pediatric narcolepsy. We also have research and development expenses related to our team of Medical Science Liaisons ("MSLs") who interact with key opinion leaders, with a focus on the science, the role of histamine in sleep-wake state stability and the novel mechanism of action of pitolisant. In addition, our MSLs support our market access team with clinical data presentations to payors upon request. Research and development costs are expensed as incurred. We expect to significantly increase our research and development efforts as we advance our clinical programs in patients with PWS, DM and pediatric narcolepsy, and continue to expand our product-candidate pipeline. Research and development expenses include:

- employee-related expenses, such as salaries, share-based compensation, benefits and travel expenses for our research and development personnel;
- direct third-party costs such as expenses incurred under agreements with CROs, and contract manufacturing organizations ("CMOs");
- manufacturing costs in connection with producing materials for use in conducting clinical trials; other third-party expenses directly attributable to the development of our product candidates; and

- amortization expense for assets used in research and development activities.

Currently, WAKIX is our only product and we do not currently track our internal research and development expenses on an indication-by-indication basis as they primarily relate to personnel, early research and consumable costs, which are deployed across multiple programs. A significant portion of our research and development costs are external costs, such as fees paid to CROs and CMOs, central laboratories, contractors, and consultants in connection with our clinical development activities.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials, milestone payments, and the cost of submitting an NDA to the FDA (and/or other regulatory authorities). We expect our research and development expenses to be significant over the next several years as we advance our current clinical development programs and prepare to seek regulatory approval for additional indications for pitolisant as well as potential new product candidates.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of any additional indications for pitolisant or other product candidates that we move forward for regulatory approval. There are numerous risks and uncertainties associated with developing product candidates, including uncertainty related to:

- the duration, costs and timing of clinical trials of our current development programs and any further clinical trials related to new product candidates;
- the sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- the impact of the COVID-19 pandemic on the ability to initiate new clinical trials and/or maintain the continuity of ongoing clinical trials that could be impacted by future shelter-in-place orders and needs of the health care system to focus on managing patients affected by COVID-19;
- receiving Bioprojet's consent to pursue additional indications for pitolisant;
- the acceptance of INDs for our planned clinical trials or future clinical trials;
- the successful and timely enrollment and completion of clinical trials;
- the successful completion of preclinical studies and clinical trials;
- successful data from our clinical programs that support an acceptable risk-benefit profile of our product candidates in the intended populations;
- the receipt and maintenance of regulatory and marketing approvals from applicable regulatory authorities;
- establishing agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidate is approved;
- the entry into collaborations to further the development of our product candidates;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates; and
- successfully launching our product candidates and achieving commercial sales, if and when approved.

A change in the outcome of any of these variables with respect to the development of any of our programs or any product candidate we develop would significantly change the costs, timing and viability associated with the development and/or regulatory approval of such programs or product candidates.

Sales and Marketing Expenses

Our sales and marketing expenses have primarily been limited to the market development and launch activities of WAKIX for the treatment of EDS in adult patients with narcolepsy and cataplexy in adult patients with narcolepsy. Market development and commercial launch activities account for a significant portion of the overall company operating expenses and are expensed as they are incurred. Our sales and marketing expenses are increasing in the near- and mid-term to support our indications for the treatment of EDS or cataplexy in adult patients with narcolepsy and to expand our portfolio with the anticipated growth from potential additional indications.

Sales and marketing expenses include:

- employee-related expenses, such as salaries, share-based compensation, benefits and travel expenses for our sales and marketing personnel;
- healthcare professional-related expenses, including marketing programs, healthcare professional promotional medical education, disease education, conference exhibits and market research;
- patient-related expenses, including patient awareness and education programs, disease awareness education, patient reimbursement programs, patient support services and market research;
- market access expenses, including payor education, specialty pharmacy programs and services to support the continued commercialization of WAKIX; and
- secondary data purchases (i.e. patient claims and prescription data), data warehouse development and data management.

In addition, these expenses include external costs such as website development, media placement fees, agency fees for patient, medical education and promotional expenses, market research, analysis of secondary data, conference fees, consulting fees and travel expenses.

General and Administrative Expenses

General and administrative expenses consist primarily of employee-related expenses, such as salaries, share-based compensation, benefits and travel expenses for our personnel in executive, legal, finance and accounting, human resources, investor relations, and other administrative departments. General and administrative expenses also consist of office leases, and professional fees, including legal, tax and accounting and consulting fees.

We anticipate that our general and administrative expenses will increase in the future to support our continued commercialization efforts, ongoing and future potential research and development activities, and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees paid to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with the requirements of Nasdaq and the SEC, insurance and investor relations costs. If any of our current or future indication expansion programs or new product candidates obtain U.S. regulatory approval, we expect that we would incur significantly increased expenses associated with building a sales and marketing team.

Paragon Agreements

We were party to a management services agreement (the “Management Services Agreement”) with Paragon Biosciences, LLC (“Paragon”), entered into on September 22, 2017, pursuant to which Paragon provided us with certain professional services. In exchange for services provided to us under the Management Services Agreement, we paid Paragon a management fee of $0.3 million per each calendar month. We terminated the Management Services Agreement upon the consummation of our IPO. In connection with such termination, we paid Paragon a termination fee of $2.6 million.

We are also party to a right-of-use agreement with Paragon whereby we have access to and the right to use certain office space leased by Paragon in Chicago, Illinois. For the year ended December 31, 2020, we paid fees of $0.3 million pursuant to this agreement.

Loss on Debt Extinguishment

Loss on debt extinguishment consists primarily of costs of extinguishment of debt during the period related to the prepayment of Loan Agreement with CRG.

Other Income / Expense, Net

Other income / expense, net consists primarily of costs of the fair value of the warrants associated with the Credit Agreement we entered into with OrbiMed.

Interest Income / Interest Expense

Interest income / expense, net consists primarily of interest expense on debt facilities and amortization of debt issuance costs offset by interest income earned on our cash balances.

Results of Operations

The following table sets forth selected items in our consolidated statements of operations for the periods presented:

	Year Ended December 31,	
	2020	**2019**
	(In thousands)	
Net product revenue	$ 159,742	$ 5,995
Cost of product sales	27,738	1,577
Gross profit	132,004	4,418
Operating expenses:		
Research and development	19,448	69,595
Sales and marketing	55,824	44,318
General and administrative	39,746	36,409
Total operating expenses	115,018	150,322
Operating income (loss)	16,986	(145,904)
Loss on debt extinguishment	(22,639)	—
Other expense, net	(3,071)	—
Interest expense, net	(28,220)	(6,073)
Net loss before provision for income taxes	(36,944)	(151,977)
Provision for income taxes	—	—
Net loss	$ (36,944)	$ (151,977)

Net Product Revenue

Net product revenue increased by $153.7 million, or 2,564.6%, for the year ended December 31, 2020 compared to the same period in 2019. The increase was due to the growing commercial sales of WAKIX which was launched on November 1, 2019.

Cost of Product Sales

Cost of product sales increased by $26.2 million, or 1,658.9%, for the year ended December 31, 2020 compared to the same period in 2019. The increase was due to the growing commercial sales of WAKIX, which was launched on November 1, 2019. Cost of product sales is primarily comprised of the royalty payment to Bioprojet.

Research and Development Expenses

Research and development expenses decreased by $50.1 million, or 72.1%, for the year ended December 31, 2020 as compared to the same period in 2019. The decrease was primarily due to a milestone payment in February 2019 upon the acceptance of our NDA for WAKIX by the FDA in accordance with the Bioprojet License Agreement.

Sales and Marketing Expenses

Sales and marketing expenses increased by $11.5 million, or 26.0%, for the year ended December 31, 2020 as compared to the same period in 2019. The increase was primarily due to field sales force personnel expenses and related field sales operations associated with the commercialization of WAKIX and patient engagement and marketing activities.

General and Administrative Expenses

General and administrative expenses increased by $3.3 million, or 9.2%, for the year ended December 31, 2020 as compared to the same period in 2019. This is primarily due to intangible asset amortization for a full year in 2020 and the amortization of the Cataplexy Milestone, additional fees associated with our IPO and expenses related to becoming a public company in 2020 and the termination fee in connection with the Management Services Agreement, offset by employee stock awards and the legal settlement with our former CEO.

Loss on Debt Extinguishment

Loss on debt extinguishment increased $22.6 million, or 100%, for the year ended December 31, 2020 as compared to the same period in 2019 due to costs of extinguishment of debt during the period related to the prepayment of the Loan Agreement with CRG.

Other Expense, Net

Other expense, net increased by $3.1 million, or 100%, for the year ended December 31, 2020, as compared to the same period in 2019 primarily due to the change in the fair value of warrants issued during 2020.

Interest Expense, Net

Interest expense increased by $22.1 million, or 364.7%, for the year ended December 31, 2020, as compared to the same period in 2019 primarily due to payment of interest on the Loan Agreement and amortization of debt issuance costs compared to the payment of interest on the Credit Agreement and amortization of debt issuance costs. This was partially offset by interest income earned on our cash balances.

Income Taxes

For interim periods, we estimate the annual effective income tax rate and apply the estimated rate to the year-to-date income or loss before income taxes. The effective income tax rate was 0.0% for all periods. Currently, we have recorded a full valuation allowance against our net deferred tax assets, primarily related to federal and state net operating losses.

Liquidity and Capital Resources

Overview

To date, we have financed our operations primarily with (a) proceeds from sales of our convertible preferred stock, (b) borrowings under (i) our Loan Agreement with CRG and (ii) our Credit Agreement with OrbiMed, and (c) the proceeds from our IPO. From our inception through December 31, 2020, we have received aggregate proceeds of $345.0 million from sales of our convertible preferred stock. On August 21, 2020, we completed the IPO of our common stock, in which we sold 6,151,162 shares of our common stock, including 802,325 shares of our common stock pursuant to the underwriters' over-allotment option. The shares began trading on the Nasdaq Global Market on August 19, 2020. The shares were sold at a price of $24.00 per share for net proceeds of approximately $135.4 million. As of December 31, 2020, we had cash, cash equivalents and restricted cash of $229.4 million and accumulated deficit of $488.2 million. As of December 31, 2020, we had outstanding debt, net of issuance costs, of $194.3 million.

The consolidated financial statements have been prepared as though we will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of

business. We have incurred operating losses and negative cash flows from operations since inception resulting in an accumulated deficit of $488.2 million as of December 31, 2020.

We believe that our anticipated cash from operating and financing activities and existing cash and cash equivalents will enable us to meet our operational liquidity needs and fund our planned investing activities for the next 12 months. We have based this estimate on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we expect. See "—Overview—Liquidity and Sources of Funding."

OrbiMed Credit Agreement

On February 28, 2019, we entered into the Loan Agreement with CRG for an aggregate of $200.0 million of which $102.5 million was outstanding as of December 31, 2019. On January 9, 2020, we entered into the Credit Agreement with OrbiMed for an aggregate of $200.0 million and paid off all of our obligations under the Loan Agreement. Borrowings under the Credit Agreement are collateralized by all of the Company's assets, excluding the intellectual property licensed through the Bioprojet License Agreement. At the time of prepayment or repayment of all or any portion of the principal of the OrbiMed Loan, the Company is required to pay an exit fee of 7.0% of the principal amount of the OrbiMed Loan prepaid, repaid, or required to be prepaid or repaid. The Credit Agreement matures on January 9, 2026 and bears an interest rate of the greater of (a) LIBOR or (b) 2.00% per annum, plus 11.00% per annum. When the LIBOR rate is no longer used post-2021, the Prime Rate will be used in the determination of the interest rate. The Credit Agreement requires compliance with certain financial covenants, including minimum net revenue thresholds and cash balance requirements (which include maintaining minimum liquidity of $12.5 million), and financial reporting requirements. We have been in compliance with the financial covenants under the Credit Agreement since it was entered into on January 9, 2020. The Credit Agreement also contains certain negative restrictive covenants that either limit our ability to, or require a mandatory prepayment in the event we, engage in new lines of business, incur additional indebtedness or liens, make certain investments, make certain payments, pay cash dividends, merge with other companies or consummate certain changes of control, acquire other companies, transfer or dispose of certain assets, liquidate or dissolve, amend certain material agreements, enter into sale and leaseback transactions, enter into various other specified transactions, and change our name, location, executive office or executive management without notice.

Recent Milestone Payment

Upon the Cataplexy Milestone Trigger Date, we became obligated to make the $100.0 million Cataplexy Milestone Payment to Bioprojet pursuant to the terms of the Bioprojet License Agreement. In October 2020, we made a payment to Bioprojet of $2.0 million to extend the Cataplexy Milestone Payment due date to within 90 days of the Cataplexy Milestone Trigger Date. On January 6, 2021, we made the $100.0 million Cataplexy Milestone Payment in full to Bioprojet.

Cash Flows

The following table sets forth a summary of our cash flows for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
	(In thousands)	
Selected cash flow data		
Cash provided by (used in):		
Operating activities	$ (2,985)	$ (75,436)
Investing activities	(2,002)	(127,149)
Financing activities	209,161	143,769

Operating Activities

Net cash used in operating activities decreased to $3.0 million for the year ended December 31, 2020 as compared to $75.4 million for the same period in 2019. This decrease was primarily attributable to company revenue growth associated with the commercialization of WAKIX for a full year in 2020.

Net cash used in operating activities for the year ended December 31, 2020 consisted of our net loss of $36.9 million adjusted for non-cash items of $22.6 million associated with loss on extinguishment of debt and $13.0 million related to intangible amortization and fair value of warrants.

Net cash used in operating activities for the year ended December 31, 2019 consisted of net loss of $152.0 million adjusted for a reclassification of $52.0 million to investing activities related to a milestone payment associated with the Bioprojet License Agreement, $9.9 million related to stock compensation expense, and $2.8 million of intangible amortization. Net working capital excluding cash increased $8.2 million.

Investing Activities

Net cash used in investing activities decreased to $2.0 million for the year ended December 31, 2020 as compared to $127.1 million for the same period in 2019. This change was primarily attributable to $50.0 million and $75.0 million of milestone payments associated with the Bioprojet License Agreement.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $209.2 million, which primarily consisted of $194.2 million associated with the OrbiMed Credit Agreement net of issuance costs and net proceeds from our IPO of $135.4 million, offset with $120.9 million of repayment and exit fees associated with the CRG Loan Agreement.

Net cash provided by financing activities for the year ended December 31, 2019 was $143.8 million, which primarily consisted of $94.8 million associated with the CRG Loan Agreement net of issuance costs and $48.9 million in proceeds from the issuance of our Series C Preferred Stock net of issuance costs.

Off-Balance Sheet Arrangements

As of and for the years ended December 31, 2020 and 2019, we did not have any off-balance sheet arrangements, as defined under SEC rules.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with GAAP, we evaluate our estimates and judgments on an ongoing basis.

Significant estimates include assumptions used in the determination of some of our costs incurred under our services type agreements and which costs are charged to research and development and general and administrative expense. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those under GAAP that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our accounting policies are more fully described in Note 3 to our financial statements included herein under "Part II—Item 8. Financial Statements and Supplementary Data.", we believe the following are the critical accounting policies used in the preparation of our consolidated financial statements that require significant estimates and judgments.

Revenue Recognition

Effective January 1, 2019, we adopted ASC 606, Revenue from Contracts with Customers (ASC 606), or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope

of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. We have determined that the delivery of our product to our customer constitutes a single performance obligation as there are no other promises to deliver goods or services. Shipping and handling activities are considered to be fulfilment activities and are not considered to be a separate performance obligation. We have assessed the existence of a significant financing component in the agreements with our customers. The trade payment terms with our customers do not exceed one year and therefore, no amount of consideration has been allocated as a financing component. Taxes collected related to product sales are remitted to governmental authorities and are excluded from revenue.

Product Sales, Net

We began commercial sales of WAKIX in November 2019. We sell WAKIX to our customers (a limited number of specialty distributors) that, in turn, distribute WAKIX to patients.

We recognize revenue on sales of WAKIX when the customer obtains control of the product, which occurs at a point in time, typically upon delivery. Product revenues are recorded at the product's wholesale acquisition costs, net of applicable reserves for variable consideration that are offered within contracts between us and our customers, payors, and other indirect customers relating to the sale of WAKIX. Components of variable consideration include government and commercial contracts, product returns, commercial co-payment assistance program transactions, and distribution service fees. These deductions, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as a current liability or reduction of receivables, based on the expected value method and a range of outcomes and are probability weighted in accordance with ASC 606.

The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under contracts will not occur in a future period. Our analyses contemplate the application of the constraint in accordance with ASC 606. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Government Contracts

We have entered into contracts (i) to participate in the Medicaid Drug Rebate Program and the Medicare Part D program, and (ii) to sell to the U.S. Department of Veterans Affairs, 340b entities and other government agencies, or Government Payors, so that WAKIX will be eligible for purchase by, in partial or full reimbursement from, such Government Payors. These reserves are recorded in the same period the revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included in accounts payable or accrued expenses. For Medicare Part D, we estimate the number of patients in the prescription drug coverage gap for whom we will owe a payment under the Medicare Part D program.

We estimate the rebates that we will provide to Government Payors for those programs that require rebates. These rebate estimates are based upon (i) the government-mandated discounts applicable to government-funded programs, (ii) information obtained from its customers and (iii) information obtained from other third parties regarding the payor mix for WAKIX. The liability for these rebates consists of estimates of claims for the current year and estimated future claims that will be made for product shipments that have been recognized as revenue but remain in the distribution channel inventories at the end of each reporting period.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed and some require advanced payments. We make estimates of our accrued expenses of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research services on our behalf and any clinical trials;
- investigative sites or other providers in connection with studies and any clinical trials;
- vendors in connections with the preparation of our NDA file, market and patient awareness programs, website development, market research and analysis and medical education;
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses for services rendered on our estimates of the services received and efforts expended pursuant to quotes, contracts and communicating with our vendors. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payments. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid or accrued expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We recognize stock-based compensation expense related to stock options granted to employees based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting stock-based compensation expense, for stock options that only have service vesting requirements or performance-based vesting requirements without market conditions using the Black- Scholes option-pricing model. The grant date fair value of the stock-based awards with service vesting requirements is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. Determining the appropriate amount to expense for performance-based awards based on the achievement of stated goals requires judgment. The estimate of expense is revised periodically based on the probability of achieving the required performance targets and adjustments are made as appropriate. The cumulative impact of any revisions is reflected in the period of change. If any applicable financial performance goals are not met, no compensation cost is recognized and any previously recognized compensation cost is reversed.

We recognize stock-based compensation expense related to stock options granted to non-employees issued in exchange for services based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting share-based compensation expense, using the Black-Scholes option-pricing model; however, the fair value of the stock options granted to non-employees is remeasured each reporting period until the service is complete, and the resulting increase or decrease in value, if any, is recognized as expense or a reduction in previously recognized expense, respectively, during the period the related services are rendered.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions, which determine the fair value of share- based awards. These assumptions include:

Expected term. Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and

the end of the contractual term). For stock- based awards granted to non-employees, the expected term represents the contractual term of the award.

Common stock price. Our board of directors determines the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant. Future expense amounts for any particular period could be affected by changes in our assumptions or market conditions.

Expected volatility. Prior to the initial public offering of our common stock, we were a privately held company and did not have any trading history for our common stock and the expected volatility was estimated using weighted-average measures of implied volatility and the historical volatility of our peer group of companies for a period equal to the expected life of the stock options. Our peer group of publicly traded biopharmaceutical companies was chosen based on their similar size, stage in the life cycle or area of specialty.

Risk-free interest rate. The risk-free interest rate is based on the rates paid on securities issued by the U.S. Treasury with a term approximating the expected life of the stock options.

Expected dividend. We have never paid, and do not anticipate paying, cash dividends on our common stock. Therefore, the expected dividend yield was assumed to be zero.

The following table reflects the range of assumptions used to estimate the fair value of awards.

	2020	2019
Dividend yield		0.00%0.00%
Expected volatility		55.00% - 95.80%95.30% - 99.30%
Risk-free interest rate		0.32% - 0.56%1.60% - 2.59%
Lack of marketability discount		0.00% - 20.48%26.00% - 31.00%
Expected term (years)		5.40 - 6.506.50

Common Stock Valuations

Prior to the consummation of our IPO, our common stock was not publicly traded. As such, we were required to estimate the fair value of our common stock. Our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development or commercial performance; our actual operating results and financial performance; the progress of our commercialization and research and development efforts; conditions in the industry and economy in general; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or a sale of our company, given prevailing market conditions; equity market conditions affecting comparable public companies; the lack of marketability of our common stock and the results of independent third party valuations. Our board of directors also took into consideration the valuations of our common stock that were prepared by an independent third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The assumptions underlying these valuations represented management’s best estimate, which involved inherent uncertainties and the application of management’s judgment. As a result, if we had used different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

For our valuations performed as of, and prior to, December 31, 2018, we used the Option Pricing Model Backsolve method to estimate the fair value of our common stock. In an option pricing method, or OPM, framework, the backsolve method for inferring the equity value implied by a recent financing transaction involves making assumptions for the expected time to liquidity, volatility and risk-free rate and then solving for the value of equity such that value for the most recent financing equals the amount paid. For our February 13, 2019 valuation, we used an income-based approach of a Discounted Cash Flow, or DCF, method to estimate the fair value of our common stock. The DCF method is based upon the theory that the value of a business is equal to the present value of its projected future cash flows. For our valuations performed August 14, 2019 through December 31, 2019, we used a combination of both, Backsolve and DCF, to estimate the fair value of our common stock. For our valuations performed as of March 31, 2020 and June 30, 2020, we used a DCF to estimate the fair value of our common stock. Furthermore, as of each of the valuation dates and even being an

early-stage commercial company, the future liquidity events were difficult to forecast. We applied a discount for lack of marketability to account for a lack of access to an active public market.

For valuations after the completion of the IPO, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant. Future expense amounts for any particular period could be affected by changes in our assumptions or market conditions.

Options Granted

The following table sets forth by grant date the number of shares of common stock subject to options granted from January 1, 2019 through December 31, 2020, the per share exercise price of the options, the per share fair value of the shares of common stock on each grant date and the per share estimated fair value of the options on each grant date:

Grant Date	Number of Shares Subject to Options Granted	Per Share Exercise Price of Options	Fair Value per Share on Grant Date	Per Share Estimated Fair Value of Options on Grant Date
January 7, 2019	40,166	$8.22	$4.28	$3.29
January 28, 2019	12,172	$8.22	$4.28	$3.29
February 11, 2019	2,434	$8.22	$4.28	$3.29
March 11, 2019	6,086	$8.22	$5.34	$4.11
March 25, 2019	8,520	$8.22	$5.34	$4.11
April 8, 2019	4,869	$8.22	$5.34	$4.11
April 15, 2019	37,734	$8.22	$5.34	$4.11
April 22, 2019	29,822	$8.22	$5.34	$4.11
April 29, 2019	21,909	$8.22	$5.34	$4.11
May 13, 2019	4,869	$8.22	$5.34	$4.11
May 20, 2019	13,389	$8.22	$5.34	$4.11
June 17, 2019	120,483	$8.22	$5.34	$4.11
June 24, 2019	4,868	$8.22	$5.34	$4.11
July 1, 2019	52,332	$8.22	$5.34	$4.11
August 5, 2019	8,520	$8.22	$5.34	$4.11
August 26, 2019	608	$8.22	$6.66	$5.10
September 30, 2019	3,651	$8.22	$6.66	$5.10
October 21, 2019	3,651	$8.22	$6.66	$5.10
October 28, 2019	36,518	$8.22	$6.66	$5.10
January 1, 2020	15,215	$8.22	$7.15	$5.67
January 13, 2020	608	$8.22	$7.15	$5.67
January 22, 2020	2,434	$8.22	$7.15	$5.67
February 26, 2020	3,651	$8.22	$7.15	$5.67
March 1, 2020	3,043	$8.22	$7.15	$5.67
March 2, 2020	2,434	$8.22	$7.15	$5.67
March 4, 2020	114,845	$8.22	$7.15	$5.67
March 16, 2020	10,346	$8.22	$7.15	$5.67
March 23, 2020	3,651	$8.22	$7.15	$5.67
May 7, 2020	12,172	$13.72	$13.72	$10.68
June 23, 2020	9,129	$13.72	$13.72	$10.68
August 18, 2020	2,560,230	$24.00	$24.00	$14.36
August 18, 2020	65,248	$24.00	$24.00	$13.87
November 5, 2020	34,078	$47.77	$47.77	$26.46
November 11, 2020	9,208	$47.47	$47.47	$27.15
December 10, 2020	179,979	$42.88	$42.88	$23.80

Stock Appreciation Rights Granted

The following table sets forth by grant date the number of shares of common stock subject to stock appreciation rights, or SARs, granted from January 1, 2019 through December 31, 2020, the per share base price of the SARs, the per share fair value of the shares of common stock on each grant date and the per share estimated fair value of the SARs on each grant date:

Grant Date	Number of Shares Subject to SARs Granted	Per Share Base Price of SARs	Fair Value per Share on Grant Date	Per Share Estimated Fair Value of SARs on Grant Date
January 7, 2019	40,165	$8.22	$4.28	$3.29
April 22, 2019	6,086	$8.22	$5.34	$4.11
June 23, 2020	9,129	$13.72	$13.72	$10.68

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Deferred tax assets may be reduced by a valuation allowance if, based on all available evidence, it is more likely than not that some portion or all of the deferred income tax assets will not be realized. Management judgment is required in determining the period in which a reversal of a valuation allowance should occur. We are required to consider all available evidence, both positive and negative, such as historical levels of income and future forecasts of taxable income among other items, in determining whether a full or partial release of its valuation allowance is required. Our accounting for deferred tax consequences represents the best estimate of those future events. We present deferred income taxes on the Consolidated Balance Sheet on a jurisdictional basis as either a net noncurrent asset or liability.

We record liabilities for uncertain tax positions based on a two-step approach. The first step is recognition, where we evaluate whether an individual tax position has a likelihood of greater than 50% of being sustained upon examination based solely on the technical merits of the position, including resolution of any related appeals or litigation processes. For tax positions that are currently estimated to have less than a 50% likelihood of being sustained, no tax benefit is recorded. For tax positions that have met the recognition threshold in the first step, we perform the second step of the approach of measuring the benefit (expense) to be recorded. The actual benefits (expense) ultimately realized may differ from our estimates. In future periods, changes in facts, circumstances, and new information may require us to change the recognition and measurement estimates with regard to individual tax positions. Changes in recognition and measurement estimates are recorded in the statement of income and balance sheet in the period in which such changes occur. As of December 31, 2020, and 2019, we did not have any liabilities for unrecognized tax positions. As it relates to any interest and penalties associated with any uncertain tax positions, our position is to include those interest and penalties as a component of income tax expense.

Recent Accounting Pronouncements

See Note 3 to our financial statements included herein under “Part II—Item 8. Financial Statements and Supplementary Data.” for more information.

The JOBS Act

We are an “emerging growth company”, or EGC, as defined in the Jumpstart Our Business Startups Act, or JOBS Act, of 2012. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies.

We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an EGC or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates. If we were to subsequently elect instead to comply with these public company effective dates, such election would be irrevocable pursuant to the JOBS Act.

We will remain an EGC until the earliest of (i) the last day of our fiscal year (a) following the fifth anniversary of the completion of the initial public offering of our common stock, (b) in which we have total annual gross revenues of at least $1.07 billion or (ii) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th and (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities over a three-year period.

Non-GAAP Financial Measures

In addition to our GAAP results, we provide certain non-GAAP metrics including adjusted net income and adjusted net income per share. We believe that the presentation of these measures provides important supplemental information to management and investors regarding our performance. These measurements are not a substitute for GAAP measurements, and the manner in which we calculate adjusted net income and adjusted net income per share may not be identical to the manner in which other companies calculate adjusted net income and adjusted net income per share. Management uses these non-GAAP measurements as an aid in monitoring our on-going financial performance from quarter-to-quarter and year-to-year on a regular basis and for benchmarking against comparable companies.

EBITDA is intended to provide a measure of the Company’s operating performance as it eliminates the effects of financing and capital expenditures. EBITDA consists of GAAP net loss excluding: (i) interest expense, (ii) income tax provision, (iii) depreciation and (iv) amortization of intangibles.

Non-GAAP adjusted net income (loss) and non-GAAP adjusted net income (loss) per share are intended to provide an enduring, normalized view of net income and our broader business operations that we expect to experience on an ongoing basis by removing items which may be irregular, one-time, or non-recurring from net income. This enables us to identify underlying trends in our business that could otherwise be masked by such items.

Non-GAAP adjusted net income (loss) consists of GAAP net loss excluding: (i) interest expense, (ii) income tax provision, (iii) depreciation, (iv) amortization of intangibles, (v) stock-based compensation, (vi) loss on debt extinguishment, and (vii) warrant expense.

A reconciliation of GAAP net loss to non-GAAP adjusted net income (loss) appears in the table below (in thousands except share and per share data):

	Year Ended December 31, 2020	2019
Net loss	$ (36,944)	$ (151,977)
Non-GAAP Adjustments:		
Interest expense	28,220	6,073
Taxes	—	—
Depreciation	394	395
Amortization	9,843	2,815
EBITDA	1,513	(142,694)
Additional Non-GAAP Adjustments:		
Stock-based compensation expense	5,190	9,909
Loss on debt extinguishment	22,639	—
Warrant expense	3,109	—
Non-GAAP adjusted net income (loss)	$ 32,451	$ (132,785)
Accumulation of yield on preferred stock	(26,904)	(35,231)
Non-GAAP adjusted net income (loss) available to common stockholders	5,547	(168,016)
GAAP reported net loss per diluted share	$ (2.48)	$ (24.07)
Non-GAAP adjusted net income (loss) per diluted share	$ 0.21	$ (21.60)
Weighted average number of shares of common stock used in non-GAAP diluted per share	26,982,978	7,777,441

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2020, our cash and cash equivalents consisted of cash and money market accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, an immediate 10% change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

As of December 31, 2020, we had $200.0 million in borrowings outstanding. The term loan bears interest at an interest rate of the greater of (a) LIBOR or (b) 2.00% per annum, plus 11.00% per annum. Based on the $200.0 million of principal outstanding as of December 31, 2020, an immediate 10% change in the Prime Rate would not have a material impact on our debt-related obligations, financial position or results of operations.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations for the years ended December 31, 2020 or 2019.

Item 8. Financial Statements and Supplementary Data.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Harmony Biosciences Holdings, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Harmony Biosciences Holdings, Inc. and subsidiary (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Chicago, Illinois
March 25, 2021

We have served as the Company's auditor since 2017.

HARMONY BIOSCIENCES HOLDINGS, INC. AND SUBSIDIARY
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2020	December 31, 2019
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 228,631	$ 24,457
Trade receivables, net	22,176	4,255
Inventory, net	3,823	1,088
Prepaid expenses	6,959	1,436
Other current assets	1,302	261
Total current assets	262,891	31,497
NONCURRENT ASSETS:		
Property and equipment, net	938	1,330
Restricted cash	750	750
Intangible asset, net	162,343	72,185
Other noncurrent assets	152	941
Total noncurrent assets	164,183	75,206
TOTAL ASSETS	$ 427,074	$ 106,703
LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Trade payables	$ 2,556	$ 6,360
Accrued compensation	8,942	7,917
Accrued expenses	122,727	5,500
Other current liabilities	314	115
Total current liabilities	134,539	19,892
NONCURRENT LIABILITIES:		
Deferred rent	212	287
Long term debt, net	194,250	97,946
Other noncurrent liabilities	893	163
Total noncurrent liabilities	195,355	98,396
TOTAL LIABILITIES	329,894	118,288
COMMITMENTS AND CONTINGENCIES (Note 9)		
CONVERTIBLE PREFERRED STOCK		
Convertible preferred stock, net of placement costs		
Series A convertible preferred stock - $1.00 stated value; 0 shares and 286,000,000 shares authorized at December 31, 2020 and 2019, respectively; 0 shares and 285,000,000 shares issued and outstanding at December 31, 2020 and 2019, respectively	—	348,203
Series B convertible preferred stock - $1.25 stated value; 0 shares and 8,030,000 shares authorized at December 31, 2020 and 2019, respectively; 0 shares and 8,000,000 shares issued and outstanding at December 31, 2020 and 2019, respectively	—	12,023
Series C convertible preferred stock - $1.96 stated value; 0 shares and 25,600,000 shares authorized at December 31, 2020 and 2019, respectively; 0 shares and 25,510,205 shares issued and outstanding at December 31, 2020 and 2019, respectively	—	51,051
STOCKHOLDERS' EQUITY (DEFICIT):		
Preferred stock - $0.00001 par value; 10,000,000 shares and 0 shares authorized at December 31, 2020 and 2019, respectively; 0 shares issued and outstanding at December 31, 2020 and 2019, respectively	—	—
Common stock—$0.00001 par value; 500,000,000 shares and 423,630,000 shares authorized at December 31, 2020 and 2019, respectively; 56,890,569 shares and 7,787,470 issued and outstanding at December 31, 2020 and 2019, respectively	1	—
Additional paid in capital	585,374	—
Accumulated deficit	(488,195)	(422,862)
TOTAL STOCKHOLDERS' EQUITY (DEFICIT)	97,180	(422,862)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY (DEFICIT)	$ 427,074	$ 106,703

The accompanying notes are an integral part of the consolidated financial statements

HARMONY BIOSCIENCES HOLDINGS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2020	**2019**
Net product revenues	$ 159,742	$ 5,995
Cost of product sold	27,738	1,577
Gross profit	132,004	4,418
Operating expenses:		
Research and development	19,448	69,595
Sales and marketing	55,824	44,318
General and administrative	39,746	36,409
Total operating expenses	115,018	150,322
Operating income (loss)	16,986	(145,904)
Loss on debt extinguishment	(22,639)	—
Other expense, net	(3,071)	—
Interest expense, net	(28,220)	(6,073)
Loss before income taxes	(36,944)	(151,977)
Income taxes	—	—
Net loss and comprehensive loss	$ (36,944)	$ (151,977)
Accumulation of dividends on preferred stock	(26,904)	(35,231)
Net loss available to common stockholders	$ (63,848)	$ (187,208)
NET LOSS PER SHARE:		
Basic	$ (2.48)	$ (24.07)
Diluted	$ (2.48)	$ (24.07)
Weighted average number of shares of common stock - basic	25,772,419	7,777,441
Weighted average number of shares of common stock - diluted	25,772,419	7,777,441

The accompanying notes are an integral part of the consolidated financial statements

HARMONY BIOSCIENCES HOLDINGS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share and per share data)

	Convertible Preferred Stock Series A, B, & C		Common Stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares (1)	Amount			
Balance as of December 31, 2018	293,000,000	$ 324,201	7,777,100	$ —	$ —	$ (242,673)	$ (242,673)
Net loss	—	—	—	—	—	(151,977)	(151,977)
Issuance of Series C convertible preferred stock, net of issuance costs	25,510,205	48,868	—	—	—	—	—
Preferred stock dividend, Series A	—	32,160	—	—	(9,994)	(22,166)	(32,160)
Preferred stock accretion, Series A	—	2,742	—	—	—	(2,742)	(2,742)
Preferred stock dividend, Series B	—	1,098	—	—	—	(1,098)	(1,098)
Preferred stock accretion, Series B	—	22	—	—	—	(22)	(22)
Preferred stock dividend, Series C	—	1,973	—	—	—	(1,973)	(1,973)
Preferred stock accretion, Series C	—	211	—	—	—	(211)	(211)
Exercise of stock options	—	—	10,370	—	85	—	85
Stock-based compensation	—	—	—	—	9,909	—	9,909
Balance as of December 31, 2019	318,510,205	$ 411,275	7,787,470	$ —	$ —	$ (422,862)	$ (422,862)
Net loss	—	—	—	—	—	(36,944)	(36,944)
Preferred stock dividend, Series A	—	22,780	—	—	(1,048)	(21,732)	(22,780)
Preferred stock accretion, Series A	—	5,562	—	—	(3,572)	(1,990)	(5,562)
Preferred stock dividend, Series B	—	777	—	—	1	(778)	(777)
Preferred stock accretion, Series B	—	53	—	—	(37)	(16)	(53)
Preferred stock dividend, Series C	—	3,347	—	—	—	(3,347)	(3,347)
Preferred stock accretion, Series C	—	921	—	—	(563)	(359)	(922)
Issuance of stock upon initial public offering, net of issuance costs	—	—	6,151,162	—	135,435	—	135,435
Conversion of Series A, B, C convertible stock to common stock	(318,510,205)	(444,715)	42,926,630	1	444,715	—	444,716
Reclassification of warrant liability to equity	—	—	—	—	5,468	—	5,468
Exercise of options	—	—	37,947	—	299	—	299
Stock-based compensation	—	—	—	—	4,693	—	4,693
Repurchase and cancellation of common units	—	—	(12,175)	—	—	(167)	(167)
Repurchase and cancellation of common units withheld for taxes	—	—	(465)	—	(17)	—	(17)
Balance as of December 31, 2020	—	$ —	56,890,569	$ 1	$ 585,374	$ (488,195)	$ 97,180

(1) Common stock of Harmony Biosciences Holdings, Inc.

The accompanying notes are an integral part of the consolidated financial statements

HARMONY BIOSCIENCES HOLDINGS, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands, except share and per share data)

	Year Ended December 31, 2020	2019
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (36,944)	$ (151,977)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	394	395
Intangible amortization	9,843	2,815
Milestones associated with acquired in-process research & development (IPR&D)	2,000	52,000
Stock-based compensation expense	4,693	9,909
Stock appreciation rights market adjustment	497	—
Warrant expense	3,109	—
Noncash paid-in-kind interest expense	—	2,538
Debt issuance costs amortization	2,412	592
Loss on debt extinguishment	22,639	—
Change in operating assets and liabilities:		
Trade receivables	(17,922)	(4,255)
Inventory	(2,735)	(1,088)
Prepaid expenses and other assets	(6,563)	1,467
Other non-current assets	789	(420)
Trade payables	(3,804)	4,898
Accrued expenses and other current liabilities	18,450	7,763
Other non-current liabilities	157	(73)
Net cash used in operating activities	(2,985)	(75,436)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of property and equipment	(2)	(149)
Milestone associated with acquired in-process research & development (IPR&D)	(2,000)	(52,000)
Milestone and acquisition of intangible asset	—	(75,000)
Net cash used in investing activities	(2,002)	(127,149)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock upon initial public offering	147,628	—
Initial public offering issuance costs	(12,193)	—
Proceeds from issuance of preferred stock	—	50,000
Preferred stock issuance costs	—	(1,132)
Proceeds from long term debt	200,000	100,000
Debt issuance costs	(5,804)	(5,184)
Extinguishment of debt	(102,538)	—
Extinguishment of debt exit fees	(18,047)	—
Proceeds from exercised options	299	85
Repurchase of common stock	(167)	—
Tax payments for employees shares withheld	(17)	—
Net cash provided by financing activities	209,161	143,769
NET INCREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	204,174	(58,816)
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH—Beginning of period	25,207	84,023
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH—End of period	$ 229,381	$ 25,207
Supplemental Disclosure of Cash Flow Information:		
Cash paid during the year for interest	$ 26,203	$ 4,230
Cash paid during the year for milestones	2,000	127,000
Supplemental Disclosures of Noncash Investing and Financing Activities:		
Series A Preferred Stock accrued return	22,780	32,160
Series A accretion of issuance costs	5,562	2,742
Series B Preferred Stock accrued return	777	1,098
Series B accretion of issuance costs	53	22
Series C Preferred Stock accrued return	3,347	1,973
Series C accretion of issuance costs	921	211
Warrant financing	2,359	—
Warrant liability reclassified to equity	5,468	—

The accompanying notes are an integral part of the consolidated financial statements

HARMONY BIOSCIENCES HOLDINGS, INC. AND SUBSIDIARY
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except share and per share data)

1. ORGANIZATION AND DESCRIPTION OF BUSINESS

The Company

Our operating subsidiary, Harmony Biosciences, LLC, was formed on May 17, 2017. Harmony Biosciences Holdings, Inc. (the "Company") was founded on July 25, 2017 as Harmony Biosciences II, LLC, a Delaware limited liability company, and the Company converted to a Delaware corporation named Harmony Biosciences II, Inc. on September 19, 2017. On February 3, 2020, the Company changed its name to Harmony Biosciences Holdings, Inc. The Company is a holding company and has no operations. The Company's operations are conducted in its wholly owned subsidiary, Harmony Biosciences, LLC ("Harmony"). The Company is a commercial-stage pharmaceutical company focused on developing and commercializing innovative therapies for patients living with rare neurological disorders who have unmet medical needs. The Company is headquartered in Plymouth Meeting, Pennsylvania.

Initial Public Offering

On August 21, 2020, the Company completed its initial public offering ("IPO") of common stock, in which it sold 6,151,162 shares, including 802,325 shares pursuant to the underwriters' over-allotment option. The shares began trading on the Nasdaq Global Market on August 19, 2020. The shares were sold at an IPO price of $24.00 per share for net proceeds of approximately $135,435, after deducting underwriting discounts and commissions and offering expenses of approximately $12,193 payable by the Company. Upon the closing of the IPO, all outstanding shares of the Company's convertible preferred stock were automatically converted into shares of common stock and the accrued dividend payable to holders of the convertible preferred stock was paid out in shares of common stock, resulting in a total of 42,926,630 shares of common stock being issued to former holders of the Company's convertible preferred stock. Warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for a total of 410,239 shares of common stock.

Reverse Stock Split

On August 11, 2020, the Company implemented a 1-for-8.215 reverse stock split of the Company's common stock. All share and per share data shown in the accompanying financial statements and related notes have been retroactively revised to reflect the reverse stock split. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities. Shares of common stock reserved for issuance upon the conversion of the Company's Preferred Stock and preferred dividend were proportionately reduced. All references in the accompanying consolidated financial statements and related notes to the number of shares of common stock, convertible preferred stock, warrants and options to purchase common stock and per share data reflect the effect of the reverse stock split.

2. LIQUIDITY AND CAPITAL RESOURCES

The consolidated financial statements have been prepared as though the Company will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The Company has incurred operating losses and negative cash flows from operations since inception resulting in an accumulated deficit of $488,195 and $422,862, as of December 31, 2020 and 2019, respectively. As of December 31, 2020, the Company had cash and cash equivalents of $228,631.

On August 21, 2020, the Company received aggregate proceeds from a common stock offering of approximately $135,435, net of underwriting discounts and commissions and other estimated offering expenses (see Note 11). Additionally, on January 9, 2020, the Company received aggregate proceeds of approximately $200,000 through the loan agreement with OrbiMed Royalty & Credit Opportunities, LP. This capital raise and debt issuance has resolved the Company's significant risks and uncertainties regarding sources of liquidity, which previously raised substantial doubt about the Company's ability to continue as a going concern.

The Company believes that its anticipated cash from operating and financing activities and existing cash and cash equivalents will enable the Company to meet its operational liquidity needs and fund its planned investing activities for the next twelve months from the date of issuance of these consolidated financial statements.

3. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. All intercompany accounts and transactions have been eliminated in consolidation.

Significant Risks and Uncertainties

The Company's operations are subject to a number of factors that can affect its operating results and financial condition. Such factors include, but are not limited to, the results of clinical testing and trial activities of the Company's product candidates; the Company's ability to obtain regulatory approval to market its products; competition from products manufactured and sold or being developed by other companies; the price of, and demand for, the Company's products, if approved; the Company's ability to negotiate favorable licensing or other manufacturing and marketing agreements for its product candidates; and the Company's ability to raise capital.

The Company currently has one commercially approved product, WAKIX, and there can be no assurance that the Company's research and development and clinical trials will result in any successfully commercialized products in addition to WAKIX. Developing and commercializing a product requires significant time and capital and is subject to regulatory review and approval as well as competition from other biotechnology and pharmaceutical companies. The Company operates in an environment of rapid change and is dependent upon the continued services of its employees and consultants and obtaining and protecting intellectual property.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts and disclosures in the Consolidated Financial Statements, including the notes thereto, and elsewhere in this report. Uncertainties related to the magnitude and duration of COVID-19, the extent to which it will impact our estimated future financial results, worldwide macroeconomic conditions including interest rates, employment rates, consumer spending and health insurance coverage, the speed of the anticipated recovery and governmental and business reactions to the pandemic have increased the complexity of developing these estimates, including the carrying amounts of long-lived assets, and the intangible asset. Actual results may differ significantly from our estimates, including as a result of COVID-19.

Operating Segments

The Company holds all its tangible assets, conducts its operations, and revenues are generated in the U.S. Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Makers in deciding how to allocate resources to an individual segment and in assessing performance. The Company has determined it operates in a single operating segment and has one reportable segment.

Fair Value of Financial Instruments

The Company's consolidated financial statements include cash, cash equivalents, accounts payable, and accrued liabilities, all of which are short term in nature and, accordingly, approximate fair value. Additionally, prior to the IPO, the Company's consolidated financial statements included a warrant liability that was carried at fair value and was re-measured at each balance sheet date until it would be exercised or expired. In connection with the IPO, the Warrants were re-evaluated under the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 480 *Distinguishing Liabilities from Equity* and reclassified to equity. See Note 13 for a further discussion of the warrants.

It is the Company's policy, in general, to measure non-financial assets and liabilities at fair value on a nonrecurring basis. The instruments are not measured at fair value on an ongoing basis but are subject to fair value adjustments in certain circumstances (such as evidence of impairment), which, if material, are disclosed in the accompanying footnotes.

The Company measures certain assets and liabilities at fair value in accordance with ASC 820, *Fair Value Measurements and Disclosures*. ASC 820 defines fair value as the price that would be received to sell an asset or paid to transfer a liability (the exit price) in an orderly transaction between market participants at the measurement date. The guidance in ASC 820 outlines a valuation framework and creates a fair value hierarchy that serves to increase the consistency and comparability of fair value measurements and the related disclosures. In determining fair value, the Company maximizes the use of quoted prices and observable inputs. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from independent sources. The fair value hierarchy is broken down into three levels based on the source of inputs as follows:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2—Valuations based on observable inputs and quoted prices in active markets for similar assets and liabilities.

Level 3—Valuations based on unobservable inputs and models that are supported by little or no market activity.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents consist of cash and, if applicable, highly liquid investments with an original maturity of three months or less when purchased, including investments in Money Market Funds. The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the balance sheet that equal the amount reflected in the statements of cash flows.

	As of	
	December 31, 2020	**December 31, 2019**
Cash and cash equivalents	$ 228,631	$ 24,457
Restricted cash	750	750
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 229,381	$ 25,207

Amounts included in restricted cash represent those amounts required to be held as a security deposit in the form of letters of credit for the Company's credit card program and the fleet program.

Concentrations of Risk

Substantially all of the Company's cash and money market funds are held with a single financial institution. Due to its size, the Company believes this financial institution represents minimal credit risk. Deposits in this institution may exceed the amount of insurance provided on such deposits by the Federal Deposit Insurance Corporation for U.S. institutions. The Company has not experienced any losses on its deposits of cash and cash equivalents. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

The Company is also subject to credit risk from its trade receivables related to its product sales. The Company monitors its exposure within accounts receivable and records a reserve against uncollectible accounts receivable as necessary. The Company extends credit to specialty pharmaceutical distribution companies within

the United States. Customer creditworthiness is monitored and collateral is not required. Historically, the Company has not experienced credit losses on its accounts receivable. As of December 31, 2020, three customers accounted for 100% of gross accounts receivable, Caremark LLC ("CVS Caremark"), which accounted for 44% of gross accounts receivable; PANTHERx Specialty Pharmacy LLC ("Pantherx"), which accounted for 23% of gross accounts receivable; and Accredo Health Group, Inc. ("Accredo"), which accounted for 33% of gross accounts receivable. As of December 31, 2019, two customers accounted for 91% of gross accounts receivable; CVS Caremark, which accounted for 72% of gross accounts receivable, and Pantherx, which accounted for 19% of gross accounts receivable.

For the year ended December 31, 2020, three customers accounted for 100% of gross product revenues; CVS Caremark accounted for 40% of gross product revenues; Pantherx accounted for 33% of gross product revenues; and Accredo accounted for 27% of gross product revenues. For the year ended December 31, 2019 two customers accounted for 88% of gross product revenues, CVS Caremark accounted for 59% of gross product revenues and Pantherx accounted for 29% of gross product revenues.

The Company depends on a single source supplier for its product, product candidates and their active pharmaceutical ingredient.

Inventory

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on our estimates of future demand for a particular product. If our estimate of future demand changes, we consider the impact on the reserve for excess inventory and adjust the reserve as required. Increases in the reserve are recorded as charges in cost of product sales.

We capitalize inventory costs associated with our products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns, potential labeling restrictions, and any other impediments to obtaining regulatory approval. We did not capitalize preapproval inventory during 2019.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally between three and ten years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life of the asset or the term of the lease. The Company's leasehold improvements primarily relate to its new corporate headquarters in Plymouth Meeting, PA, and are generally being amortized through the end of the lease term in May 2024. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in the statement of operations and comprehensive loss in the period realized.

Intangible Asset

Intangible assets with finite useful lives consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives. The estimated useful lives associated with finite-lived intangible assets are consistent with the estimated lives of the associated products and may be modified when circumstances warrant. Such assets are reviewed for impairment when events or circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset and its eventual disposition are less than its carrying amount. The amount of any impairment is measured as the difference between the carrying amount and the fair value of the impaired asset.

Revenue Recognition

Effective January 1, 2019, the Company adopted ASC 606, Revenue from Contracts with Customers (ASC 606). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company applies the five-step model to contracts when it is probable that it will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determine those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. The Company has determined that the delivery of its product to its customer constitutes a single performance obligation as there are no other promises to deliver goods or services. Shipping and handling activities are considered to be fulfillment activities and are not considered to be a separate performance obligation. The Company has assessed the existence of a significant financing component in the agreements with its customers. The trade payment terms with its customers do not exceed one year and therefore, no amount of consideration has been allocated as a financing component. Taxes collected related to product sales are remitted to governmental authorities and are excluded from revenue.

Product Sales, Net

The Company began commercial sales of WAKIX in November 2019. The Company sells WAKIX to its customers (a limited number of specialty distributors) that, in turn, distribute WAKIX to patients.

The Company recognizes revenue on sales of WAKIX when the customer obtains control of the product, which occurs at a point in time, typically upon delivery. Product revenues are recorded at the product's wholesale acquisition costs, net of applicable reserves for variable consideration that are offered within contracts between the Company and its customers, payors, and other indirect customers relating to the sale of WAKIX. Components of variable consideration include government and commercial contracts, product returns, commercial co-payment assistance program transactions, and distribution services fees. These deductions are based on the amounts earned or to be claimed on the related sales and are classified as a current liability or reduction of receivables, based on expected value method and a range of outcomes and are probability weighted in accordance with ASC 606.

The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognition under contracts will not occur in a future period. The Company's analyses contemplate the application of the constraint in accordance with ASC 606. Actual amounts of consideration ultimately received may differ from its estimates. If actual results in the future vary from its estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Cost of Product Sold

Cost of product sold includes manufacturing and distribution costs, the cost of drug substance, FDA program fees, royalties due to third parties on net product sales, freight, shipping, handling, storage costs, and salaries of employees involved with production. The Company began capitalizing inventory upon FDA approval of WAKIX with a portion of the inventory sold during the year ended December 31, 2020 produced prior to FDA approval and, therefore, was previously expensed as research and development expense in 2019 in the amount of $1,323. Excluded from cost of product sold shown and included in general and administrative on the

consolidated statements of operations and comprehensive loss is amortization of acquired developed technology of $9,843 and $2,815 for the years ended December 31, 2020 and 2019, respectively.

Research and Development Expenses

Research and development costs are expensed as incurred. Liabilities due to third parties in connection with research and development collaborations prior to regulatory approval are expensed as incurred.

Upfront payments and pre-FDA approval milestone payments made for licensing of technology are expensed as research and development in the period in which they are incurred. Advance payments for goods and services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Advertising Expenses

We expensed the costs of advertising, including promotional expenses, as incurred. Advertising expense was $13,301 and $7,072 a for the years ended December 31, 2020 and 2019, respectively.

Stock-Based Compensation

The Company recognizes compensation expense relating to stock-based payment transactions in operating results using a fair value measurement method, in accordance with FASB ASC 718, Compensation-Stock Compensation. ASC 718 requires all stock-based payments to employees to be recognized in operating results as compensation expense based on fair value over the requisite service period of the awards. The vesting periods have a time-based provision consisting of three to five years and expire no more than 10 years after the date of grant. Upon a change of control, certain unvested awards will immediately vest. The Company determines the fair value of stock-based awards using the Black-Scholes option-pricing model, which uses both historical and current market data to estimate fair value. The method incorporates various assumptions, such as the risk-free interest rate, expected volatility, expected dividend yield, and expected life of the options.

On January 1, 2019, the Company early adopted and accounts for stock-based payments granted to nonemployees in accordance with ASU 2018-07, Compensation – Stock Compensation (ASC 718): Improvements to Nonemployee Share – Based Payment Accounting. The Company determines the fair value of the stock-based payment as the fair value of the equity instruments issued. It is measured on the grant date.

The Company also had nonemployee stock awards subject to a performance condition that are recognized based on probable outcome. On November 15, 2019 the Company modified the award to remove the performance condition resulting in $8,400 of noncash expense that is included in the Company’s consolidated results of operations for the year ended December 31, 2019 (see Note 13 for further details).

Basic and Diluted Net Loss per Share

Basic net loss per share is determined using the weighted average number of shares of common stock outstanding during each period. Diluted net income per share includes the effect, if any, from the potential exercise or conversion of securities, such as convertible preferred stock and stock options, which would result in the issuance of incremental shares of common stock. The computation of diluted net loss per shares does not include the conversion of securities that would have an anti-dilutive effect. The basic and diluted computations of net loss per share for the Company are the same because the effects of the Company’s convertible securities would be anti-dilutive (see Note 14 for further detail).

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Deferred tax assets may be reduced by a valuation allowance if, based on all available evidence, it is more likely than not that some portion or all of the deferred income tax assets will not be realized. Management judgment is required in determining the period in which a reversal of a valuation allowance should occur. The Company is required to consider all available evidence, both positive and negative, such as historical levels of income and future forecasts of taxable income among other items, in determining whether a full or partial release of its valuation allowance is required. The Company's accounting for deferred tax consequences represents the best estimate of those future events. The Company presents deferred income taxes on the Consolidated Balance Sheet on a jurisdictional basis as either a net noncurrent asset or liability.

The Company recognizes the effect of income tax positions only if those positions are more likely than not sustainable, based solely on its technical merits and consideration of the relevant taxing authority's widely understood administrative practices and precedents. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which a change in judgment occurs. At December 31, 2020 and 2019, the Company did not have any unrecognized uncertain tax positions. The Company's policy is to include any interest and penalties as a component of income tax expense.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued amended guidance to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities in the balance sheet and disclosing key information about leasing arrangements. The new guidance clarifies the criteria for distinguishing between a finance lease and operating lease, as well as classification between the two types of leases, which is substantially unchanged from the previous lease guidance. Further, the new guidance requires a lessee to recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset, initially measured at the present value of the lease payments. For finance leases, a lessee should recognize interest on the lease liability separately from amortization of the right-of-use asset. For operating leases, a lessee should recognize a single lease cost, calculated so that the cost of the lease is allocated over the lease term on a generally straight-line basis. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election not to recognize lease assets and lease liabilities. The new standard will become effective for the Company's fiscal year ending December 31, 2022. The Company is currently assessing the impact of this amended guidance and the timing of adoption.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. ASU No. 2016-13 introduces an approach, based on expected losses, to estimate credit losses on certain types of financial instruments and modifies the impairment model for available-for-sale debt securities. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2022 for companies deemed to be small reporting companies as of November 15, 2019, with early adoption permitted. The Company is currently evaluating the potential impact of adoption of this standard on its results of operations, financial position and cash flows and related disclosures.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, which simplifies the accounting for income taxes by removing certain exceptions to the general principles in the existing guidance for income taxes and making other minor improvements. The amendments are effective for annual reporting periods beginning after December 15, 2020 with early adoption permitted. The Company is currently evaluating the impact of adopting this new accounting guidance.

In March 2020, the FASB issued ASU No. 2020-04, *Reference Rate Reform (Topic 848)*, which provides guidance related to reference rate reform. The pronouncement provides temporary optional expedients and exceptions to the current guidance on contract modifications and hedge accounting to ease the financial reporting burden related to the expected market transition from the London Interbank Offered Rate ("LIBOR") and other interbank offered rates to alternative reference rates. The guidance was effective upon issuance and generally can be applied to applicable contract modifications through December 31, 2022. We are currently evaluating the impact of the transition from LIBOR to alternative reference rates but do not expect a significant impact to our consolidated financial statements.

4. INVENTORY

Inventory, net consisted of the following:

	As of	
	December 31, 2020	**December 31, 2019**
Raw materials	$ 396	$ 384
Work in process	2,660	417
Finished goods	941	287
Inventory, gross	3,997	1,088
Reserve for obsolescence	(174)	—
Total inventory, net	$ 3,823	$ 1,088

5. INTANGIBLE ASSET

On August 15, 2019, the Company received FDA approval of WAKIX® (pitolisant) for the treatment of excessive daytime sleepiness ("EDS") in adult patients with narcolepsy. This event triggered a milestone payment of $75,000 associated with the License Agreement which the Company capitalized as an intangible asset and paid in November of 2019. The Company determined a useful life of 10 years for such intangible asset, and, as of December 31, 2020 the remaining useful life was 9 years. Prior to this event, all other milestones associated with the License Agreement were expensed through research and development as they did not meet the criteria to be recognized as an intangible asset.

On October 13, 2020, the Company received notice that the FDA approved the NDA for WAKIX® for the treatment of cataplexy in adult patients with narcolepsy. This event triggered a milestone payment of $100,000 associated with the License Agreement which the Company capitalized as an intangible asset and paid in January of 2021. The Company determined a useful life of 9 years for such intangible asset, and, as of December 31, 2020 the remaining useful life was 9 years.

The Company expects the future annual amortization expense for the unamortized intangible assets to be as follows:

Years ending December 31,	
2021	$ 18,569
2022	18,569
2023	18,569
2024	18,569
2025	18,569
Total	$ 92,845

The gross carrying amount and net book value of the intangible asset is as follows:

	As of	
	December 31, 2020	December 31, 2019
Gross Carrying Amount	$ 175,000	$ 75,000
Accumulated Amortization	(12,657)	(2,815)
Net Book Value	$ 162,343	$ 72,185

6. LICENSE AGREEMENT

On July 28, 2017, Harmony entered into the License Agreement whereby Harmony acquired the exclusive right to commercialize the pharmaceutical compound pitolisant for the treatment, and/or prevention, of narcolepsy, obstructive sleep apnea, idiopathic hypersomnia, and Parkinson's disease as well as any other indications unanimously agreed by the parties in the United States and its territories. A milestone payment of $50,000 was due upon acceptance by the FDA of pitolisant's New Drug Application ("NDA"), which was achieved on February 12, 2019 and was expensed within research and development for the year ended December 31, 2019. A milestone payment of $77,000, including a $2,000 fee, was due upon FDA approval of WAKIX® (pitolisant) for treatment of EDS in adult patients with narcolepsy, which was achieved on August 14, 2019. The $2,000 payment and $75,000 milestone payment were paid in August and November 2019, respectively. In addition, a payment of $2,000 is due upon the FDA approval of the NDA for WAKIX® for the treatment of cataplexy in adult patients with narcolepsy (the "Trigger Date") which was paid in October 2020 and a $100,000 milestone payment which was paid in January 2021. An additional $40,000 milestone payment is due to Bioprojet upon WAKIX attaining $500,000 in aggregate net sales in the United States. The License Agreement also requires sales-based milestone payments, a fixed trademark royalty and a tiered royalty, all based on net sales, which become due and payable to Bioprojet on a quarterly basis. During the year ended December 31, 2020, the Company incurred $25,580 for sales-based, trademark and tiered royalties recognized as cost of product sold. As of December 31, 2020 and 2019, the Company had accrued $9,006 and $938, respectively, for sales-based, trademark and tiered royalties. At December 31, 2020 the Company had accrued $100,000 for the milestone payment to Bioprojet.

7. ACCRUED EXPENSES

Accrued expenses consist of the following:

	As of	
	December 31, 2020	December 31, 2019
Milestone payment	$ 100,000	$ —
Royalties due to third parties	9,006	938
Rebates and other sales deductions	7,803	713
Research and development	2,186	894
Selling and marketing	1,905	1,547
Professional fees, consulting, and other services	1,081	510
Debt issuance costs	—	638
Other expenses	746	260
	$ 122,727	$ 5,500

8. DEBT

Credit Agreements

On February 28, 2019, the Company entered into a multi-draw loan agreement with CRG Servicing LLC for an aggregate of $200,000 (the "CRG Loan"), which matured in March 2025. The Loan bore a fixed rate of 12%. The Loan agreement required compliance with certain financial covenants. The Company could draw three tranches of the Loan based on achieving specific milestones and dates. The Company could elect to pay the interest on the outstanding principal amount as follows: (i) only 7.5% of the 12% per annum in cash, paid quarterly, starting in March 2019, and (ii) 4.5% of the 12% per annum interest as compounded interest, added to

the aggregate outstanding principal balance quarterly; the amount of any such compounded interest being a paid-in-kind loan.

As of December 31, 2019, the Company had borrowed $100,000, resulting in cash proceeds received of $94,816, net of issuance costs. The issuance costs of $5,184 were being amortized over the six-year loan term of the CRG Loan. Unamortized debt issuance costs as of December 31, 2019 are $4,592 and are presented in the consolidated balance sheets as a direct deduction from the carrying value of the debt.

On January 9, 2020 the Company entered into a credit agreement with OrbiMed Royalty & Credit Opportunities, LP for an aggregate amount of $200,000 (the "OrbiMed Loan"), which matures in January 2026. Borrowings under the OrbiMed Loan are collateralized by all of the Company's assets, excluding the intellectual property licensed through the License Agreement. The OrbiMed Loan bears an interest rate equal to the sum of (i) the greater of (a) 1-month LIBOR or (b) 2.00% per annum, plus (ii) 11.00% per annum, paid in cash monthly in arrears on the last day of each month starting in January 2020. At the time of prepayment or repayment of all or any portion of the principal of the OrbiMed Loan, the Company is required to pay an exit fee of 7.0% of the principal amount of the OrbiMed Loan prepaid, repaid, or required to be prepaid or repaid. The Company recorded as a liability and debt discount the exit fee at the origination of the term loan.

In addition to entering into the OrbiMed Loan, the Company extinguished the CRG Loan which required a payoff amount of $120,893 consisting of principal repayment, interest, and exit fees. In connection with extinguishment of the CRG Loan, we recognized a loss on extinguishment of $22,639, which included an exit fee of $18,047 and the write-off of the remaining unamortized debt issuance costs of $4,592. The loss on extinguishment of debt was recorded in loss on debt extinguishment within the Company's consolidated statements of operations. The net cash received as a result of the transaction, less debt issuance costs of $5,804, was $73,313. These debt issuance costs will be amortized as additional interest expense over the six-year loan term of the OrbiMed Loan. The fair value of the OrbiMed loan as of December 31, 2020 was $245,700.

In connection with the OrbiMed Loan, the Company issued warrants (the "Warrants") to OrbiMed Royalty & Credit Opportunities, LP on January 9, 2020. See Note 13 for further discussion of the Warrants. Pursuant to the Warrants, OrbiMed Royalty & Credit Opportunities, LP, may purchase up to 410,239 shares of the Company's Common Stock for an initial exercise price of $16.10 at any time from the date of execution of the Warrants through the expiration date, defined within the Warrants as the earlier of (i) January 9, 2027 and (ii) the closing date of a Corporate Reorganization. The fair value of the Warrants using the Black-Scholes option-pricing model was $2,359 at January 9, 2020. The portion of the OrbiMed Loan proceeds allocated to the warrant liability resulted in a debt discount, which is presented in the consolidated balance sheets as a direct deduction from the carrying value of the debt and is being amortized as additional interest expense over the six-year loan term of the OrbiMed Loan. The unamortized debt discount as of December 31, 2020 is $2,097 and is presented in the consolidated balance sheets as a direct deduction from the carrying value of the debt.

The balances of the OrbiMed Loan as of December 31, 2020 and the CRG Loan as of December 31, 2019 were as follows:

	December 31, 2020	December 31, 2019
Liability component - principal	$ 200,000	$ 102,538
Exit fee	14,000	—
Unamortized debt discount associated with the exit fee, debt financing costs and discount with warrant financing	(19,750)	(4,592)
Liability component - net carrying value	$ 194,250	$ 97,946

Interest expense related to the OrbiMed Loan and CRG Loan were included in interest expense, net in the Consolidated Statements of Operations as follows:

	Year Ended December 31,	
	2020	2019
Interest on principal balance	$ 26,203	$ 4,231
Interest on PIK	—	2,538
Amortization of deferred financing costs	2,412	592
Total term loan interest expense	$ 28,615	$ 7,361

9. COMMITMENTS AND CONTINGENCIES

Litigation

From time to time, the Company is subject to claims and suits arising in the ordinary course of business. The Company accrues such liabilities when they are known, if they are deemed probable and can be reasonably estimated.

During 2019 the Company was involved in ongoing litigation with its former chief executive officer related to arbitration and the value of vested common shares. On October 24, 2019, the Company reached a settlement resulting in $3,466 of general and administrative expense reflected in the Company's consolidated results of operations for the year ended December 31, 2019.

Lease Agreements

In April 2018, the Company entered into an operating lease for approximately nine thousand square feet of office space in Northbrook, IL, which expired in January 2020.

In June 2018, the Company entered into an operating lease for approximately fifteen thousand square feet of office space in Plymouth Meeting, PA, which expires in May 2024.

In December 2020, the Company entered into an operating lease for approximately thirteen thousand square feet of additional office space in Plymouth Meeting, PA, which expires in May 2024. The term will not commence until the Company takes occupancy in mid-2021.

The terms of the lease payments provide for rental payments on a monthly basis and on a graduated scale. The Company recognizes rent expense on a straight-line basis over the lease period and has accrued for rent expense incurred but not paid. In addition, tenant improvement allowances recorded are amortized as a reduction to rent expense on a straight-line basis over the lease term. Rent expense was $686 for the year ended December 31, 2020, compared to $1,051 for the year ended December 31, 2019. The following table sets forth the lease payment obligations as of December 31, 2020, for the periods indicated below:

Years ending December 31,		
2021	$	534
2022		875
2023		892
2024		334
2025		—
Thereafter		—
Total	$	2,635

10. CONVERTIBLE PREFERRED STOCK

Upon the closing of the IPO, all outstanding shares of the Company's convertible preferred stock were automatically converted into shares of common stock and the accrued dividend payable to holders of the convertible preferred stock was paid out in shares of common stock, resulting in a total of 42,926,630 shares of common stock being issued to former holders of the Company's convertible preferred stock.

Series A Preferred Stock

On September 22, 2017, the Company issued 270,000,000 shares of Series A convertible preferred stock for a purchase price of $1.00 per share, or $270,000 in the aggregate. On January 8, 2018, the Company issued an additional 15,000,000 shares of Series A convertible preferred stock for a purchase price of $1.00 per share, or $15,000 in the aggregate. As of December 31, 2019, there were 286,000,000 Series A convertible preferred stock authorized of which 285,000,000 were issued and outstanding. Each outstanding share of Series A convertible preferred stock accrued dividends at 10% per annum of the Series A original issue price, subject to adjustment for stock splits, combinations, recapitalizations, stock dividends and similar transactions. Preferred dividends on the Series A convertible preferred stock were cumulative and were compounded annually.

Series B Preferred Stock

On January 8, 2018, the Company issued 8,000,000 shares of Series B convertible preferred stock for a purchase price of $1.25 per share, or $10,000 in the aggregate. As of December 31, 2019, there were 8,030,000 shares of Series B convertible preferred stock authorized, of which 8,000,000 were issued and outstanding. Each outstanding share of Series B convertible preferred stock accrued dividends at 10% per annum of the Series B original issue price, subject to adjustment for stock splits, combinations, recapitalizations, stock dividends and similar transactions. Preferred dividends on the Series B convertible preferred stock were cumulative and were compounded annually.

Series C Preferred Stock

On August 9, 2019, the Company issued 25,510,205 shares of Series C convertible preferred stock for a purchase price of $1.96 per share, or $50,000 in the aggregate. As December 31, 2019, there were 25,600,000 shares of Series C convertible preferred stock authorized, of which 25,510,205 were issued and outstanding. Each outstanding share of Series C convertible preferred stock accrued dividends at 10% per annum of the Series C original issue price, subject to adjustment for stock splits, combinations, recapitalizations, stock dividends and similar transactions. Preferred dividends on the Series C convertible preferred stock were cumulative and were compounded annually.

Dividends

The holders of Series A, Series B, and Series C convertible preferred stock were entitled to receive, when and if declared by the board of directors of the Company, cumulative dividends equal to a 10% per annum of Series A, Series B, and Series C convertible preferred stock. In addition, the holders of the outstanding shares of Series A, Series B, and Series C convertible preferred stock were entitled to receive, when and if declared by the board of directors of the Company, a dividend at least equal to any dividend payable on the Company's common stock as if all convertible preferred stock had been converted to common stock. No dividends were declared as of December 31, 2019. As part of the Company's IPO, the Company's accrued cumulative dividend was paid out to holders of Series A, Series B, and Series C convertible preferred stock in shares of the Company's common stock and reflects the reverse stock split in connection with the mandatory conversion of the Series A, Series B, and Series C convertible preferred stock into shares of the Company's common stock.

11. STOCKHOLDERS' EQUITY (DEFICIT)

Common Stock

On August 11, 2020, the Company implemented a 1-for-8.215 reverse stock split of the Company's common stock. All share and per share data shown in the accompanying financial statements and related notes have been retroactively revised to reflect the reverse stock split with the exception of the preferred stock. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities. Shares of common stock reserved for issuance upon the conversion of the Company's Preferred Stock were proportionately reduced. As of August 11, 2020, all outstanding shares of preferred stock and preferred stock dividend were convertible into shares of common stock on a 1-for-8.215 basis. On August 21, 2020, the Company completed its IPO of common stock, in which it sold 6,151,162 shares, including 802,325 shares pursuant to the underwriters' over-allotment option. The shares began trading on the Nasdaq Global Market on August 19, 2020. The shares were sold at an IPO price of $24.00 per share for net proceeds of approximately $135,435, after deducting underwriting discounts and commissions and offering expenses of approximately $12,193 incurred by the Company.

The holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of the Company's stockholders. The holders of common stock do not have any cumulative voting rights. Holders of common stock are entitled to receive ratably any dividends declared by the Company's board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. The Company's common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

1,217,285 common shares held by an investor were subject to certain forfeiture provisions that are dependent upon the outcome of certain future events. On November 15, 2019, the Company removed the

provision associated with this forfeiture resulting in $8,400 of noncash stock compensation expense reflected in the Company's consolidated results of operations for the year ended December 31, 2019.

12. STOCK INCENTIVE PLAN AND STOCK-BASED COMPENSATION

Stock Incentive Plan

On August 7, 2017, the Company adopted an equity incentive plan (the "2017 Plan"). Under the 2017 Plan, directors, officers, employees, consultants, and advisors of the Company can be paid incentive compensation measured by the value of the Company's common shares through grants of stock options, stock appreciation rights, or restricted stock.

In connection with the Company's IPO, the board of directors adopted, and its stockholders approved, the 2020 Incentive Award Plan (the "2020 Plan"), in order to facilitate the grant of cash and equity incentives to directors, employees (including the Company's named executive officers) and consultants of the Company and its subsidiaries. Upon the effectiveness of the 2020 Plan, no further grants will be made under the 2017 Plan. However, the 2017 Plan will continue to govern the terms and conditions of outstanding awards granted under it. The 2020 Plan provides for the grant of stock options, including ISOs and NSOs, SARs, restricted stock, dividend equivalents, RSUs and other stock or cash based awards.

Stock options under the 2017 Plan and the 2020 Plan have a 10-year contractual term and vest over the vesting period specified in the applicable award agreement, at achievement of a performance requirement, or upon change of control (as defined in the applicable plan).

Changes in awards granted under the Plan as of December 31, 2020 and 2019, are as follows:

	Number of Awards		Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term
Awards outstanding—December 31, 2019	2,375,218	$	8.22	8.33
Awards issued	3,035,400	$	24.54	
Awards exercised	(37,947)	$	8.22	
Awards forfeited	(112,545)	$	10.75	
Awards outstanding—December 31, 2020	5,260,126	$	17.58	8.63

As of December 31, 2020 and 2019, stock awards issued under the 2017 and 2020 Plans of 987,538 and 573,098 common shares, respectively, were vested. The Company has elected early adoption of ASU No. 2016-09 to recognize forfeitures as they occur. As a result of the adoption, for the year ended December 31, 2020 and 2019, respectively, the Company reversed $3 and $4 out of stock-based compensation previously recorded.

Value of Stock Options

The Company has valued awards for each of the plans included herein using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, the Company estimates its expected stock volatility based on historical volatility of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for the time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The assumptions used to value the awards are summarized in the following table.

	As of			
	December 31, 2020		December 31, 2019	
Dividend yield	0.00	%	0.00	%
Expected volatility	55.00 - 95.80	%	95.30 - 99.30	%
Risk-free interest rate	0.32 - 0.56	%	1.60 - 2.59	%
Lack of marketability discount	0.00 - 20.48	%	26.00 - 31.00	%
Expected term (years)	5.4 - 6.5		6.5	

The weighted average per share fair value of awards issued under the Plan was $10.06 and $3.45 in 2020 and 2019, respectively.

Stock-based compensation expense was $5,190 and $9,909 for the years ended December 31, 2020 and 2019, respectively, and was recorded in the consolidated statements of operations and comprehensive loss in the following line items:

	Year Ended December 31,	
	2020	2019
Research and development expense	$ 586	$ 287
Sales and marketing expense	703	351
General and administrative expense	3,901	9,271
	$ 5,190	$ 9,909

Options issued under the 2017 Plan and 2020 Plan are reflected as a component of equity in these consolidated financial statements. Stock appreciation rights are reflected as other non-current liability. The Company will recognize compensation expense for these awards as summarized in the following table.

Years Ending December 31,	Stock Compensation Expense
2021	$ 11,046
2022	10,915
2023	9,928
2024	8,949
2025	5,003

13. WARRANTS

In connection with the OrbiMed Loan, the Company issued Warrants to OrbiMed Royalty & Credit Opportunities, LP on January 9, 2020. Pursuant to the Warrants, OrbiMed Royalty & Credit Opportunities, LP, may purchase up to 410,239 shares of the Company's Common Stock for an initial exercise price of $16.10 at any time from the date of execution of the Warrants through the expiration date, defined within the Warrants as the earlier of (i) January 9, 2027 and (ii) the closing date of a Corporate Reorganization. The fair value of the

Warrants using the Black-Scholes option-pricing model was $2,359 on January 9, 2020 and was initially recorded as a warrant liability which was included in warrant liability in the consolidated balance sheet. The portion of the OrbiMed Loan proceeds allocated to the warrant liability resulted in a debt discount, which is presented in the consolidated balance sheets as a direct deduction from the carrying value of the debt and is being amortized as additional interest expense over the six-year loan term of the OrbiMed Loan. The unamortized debt discount as of December 31, 2020 is $2,102 and is presented in the consolidated balance sheet as a direct deduction from the carrying value of the debt. During the year ended December 31, 2020, a loss of $3,109 was recorded in other expense in the consolidated statements of operations due to the change in the fair value of the warrant liability. See footnote 16 for the fair value of the Warrants.

In connection with the IPO, the financial instrument underlying the warrants was converted from the Company's Series C Preferred Stock to the Company's Common Stock. As a result of this conversion the Warrants were re-evaluated under ASC 480 Distinguishing Liabilities from Equity and ASC 815 Derivatives and Hedging and reclassified to equity.

A summary of the changes in the warrant liability for the year ended December 31, 2020 is as follows:

Balance, beginning of period	$	—
Fair Value at Issuance		2,359
Change in fair value included in the statement of operations		3,109
Reclassification to equity		(5,468)
Balance, end of period	$	—

14. EARNINGS PER SHARE

For the years ended December 31, 2020 and 2019, the Company used the two-class method to compute net loss per common share because the Company has issued securities (convertible preferred stock) that entitle the holder to participate in dividends and earnings of the Company. Under this method, net income is reduced by the amount of any dividends earned and the accretion of convertible preferred stock to its redemption value during the period. The remaining earnings (undistributed earnings) are allocated to common stock and each series of convertible preferred stock to the extent that each preferred security may share in the earnings as if all of the earnings for the period had been distributed. The total earnings allocated to common stock is then divided by the number of outstanding shares to which the earnings are allocated to determine the earnings per share. The two-class method is not applicable during periods with a net loss, as the holders of the convertible preferred stock have no obligation to fund losses.

Diluted net loss per common share is computed under the treasury stock method by using the weighted average number of shares of common stock outstanding, plus, for periods with net income attributable to common stockholders, the potential dilutive effects of stock options and warrants. In addition, the Company analyzes the potential dilutive effects of the outstanding convertible preferred stock under the 'if-converted' method when calculating diluted earnings per share, in which it is assumed that the outstanding convertible preferred stock converts into common stock at the beginning of the period or when issued if later. The Company reports the more dilutive of the approaches (treasury stock or 'if converted') as their diluted net income per share during the period.

The Company has reported a net loss for the years ended December 31, 2020 and 2019, and the weighted average number of shares utilized for basic and diluted net loss per share attributable to common stockholders are the same for these periods because all convertible preferred stock and stock options have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact. Additionally, the fair value adjustment for the warrants was excluded from the computation of diluted net loss for the year ended December 31, 2020 since the additional income would have an antidilutive impact.

The following table sets forth the computation of basic and diluted net loss per share:

	Year Ended December 31,	
	2020	2019
Numerator		
Net loss	$ (36,944)	$ (151,977)
Accumulation of dividends on preferred stock	(26,904)	(35,231)
Net loss available to common shareholders	$ (63,848)	$ (187,208)
Denominator		
Net loss per common share - basic	$ (2.48)	$ (24.07)
Net loss per common share - diluted	$ (2.48)	$ (24.07)
Weighted average number of shares of common stock - basic	25,772,419	7,777,441
Weighted average number of shares of common stock - diluted	25,772,419	7,777,441

Potential common shares issuable upon conversion of preferred stock, exercise of stock options, and exercise of warrants that are excluded from the computation of diluted weighted-average shares outstanding as well as the warrant fair value adjustments excluded from the numerator are as follows:

	Year Ended December 31,	
	2020	2019
Stock options to purchase common stock	5,260,126	2,271,632
Convertible preferred stock	—	36,891,576
Warrants	410,239	—
Total	5,670,365	39,163,208
Adjustment for warrants	$ 3,109	$ —

15. INCOME TAXES

Details of the provision for income taxes consist of the following:

	Year Ended December 31,	
	2020	2019
Federal	$ (6,416)	$ (32,508)
State	4,198	(9,641)
Valuation allowance	2,218	42,149
	$ —	$ —
Current	$ —	$ —
Deferred	(2,218)	(42,149)
Valuation allowance	2,218	42,149
Total	$ —	$ —

The reasons for the difference between the statutory federal income tax rate and the Company's effective income tax rate as of December 31, 2020 and 2019 are as follows:

	Year Ended December 31,	
	2020	2019
Federal income tax rate	21.0%	21.0%
State taxes	(11.4)	6.3
Other	(3.6)	0.4
Valuation allowance	(6.0)	(27.7)
Total	—%	—%

Significant components of the Company's deferred tax assets and liabilities as of December 31, 2020 and 2019, are as follows:

	As of December 31,			
	2020		2019	
	Assets	Liabilities	Assets	Liabilities
Acquired in-process research and development	$ 45,346	$ —	$ 50,628	$ —
Net operating loss carryforward	44,983	—	41,427	—
Accrued compensation	4,075	—	5,158	—
Credits	1,604	—	1,682	—
Disallowed interest	7,751	—	1,661	—
Deferred rent	121	—	160	—
Fixed assets	65	—	46	—
Inventory	100	—	—	—
Other	71	1,242	61	167
Total	$ 104,116	1,242	$ 100,823	167
Net deferred tax asset	$ 102,874	$ —	$ 100,656	$ —
Valuation allowance	$ (102,874)	$ —	$ (100,656)	$ —
Total	$ —	$ —	$ —	$ —

The Company has considered available positive and negative evidence to estimate if sufficient future taxable income will be generated to allow utilization of the existing deferred tax assets. The Company has incurred operating losses and negative cash flows from operations since inception. In light of these considerations, as well as the uncertainty as to when the Company might generate taxable income, the Company has recorded a full valuation allowance of $102,874, which represents an increase of $2,218 in the Company's valuation allowance from December 31, 2019 to December 31, 2020. The amount of the net deferred tax asset considered realizable could be adjusted in the future if estimates of taxable income change or if objective negative evidence in no longer present and additional weight may be given to subjective evidence.

As of December 31, 2020 and 2019, the Company has approximately $159,395 and $147,823, respectively, of federal net operating loss ("NOL") carryforward available to offset future federal taxable income. The Company also has approximately $157,743 and $139,336 of state NOL carryforwards as of December 31, 2020 and 2019, respectively, available to offset future state taxable income. All of the Company's tax years remain open to examination by federal and state taxing authorities. The Company's pre-2018 federal NOLs expire in 2037 whereas the Company's NOLs arising in 2018, and subsequent years, have an unlimited carryforward period. The Company's state NOLs begin to expire in 2037. Utilization of the net operating loss carryforwards may be subject to a substantial limitation due to ownership change limitations that may occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), as well as similar state provisions. These ownership changes may limit the amount of net operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders or public groups.

As of December 31, 2020 and 2019, the Company has federal tax credits of $1,603 and $837, respectively. These credits begin to expire in 2037.

16. FINANCIAL INSTRUMENTS

The Company primarily applies the market approach to determine the fair value of financial instruments that are measured at fair value on a recurring basis. There were no changes to its valuation techniques used to determine the fair value of financial instruments during the year ended December 31, 2020. The Company's financial assets and liabilities which are measured at fair value on a recurring basis were comprised of cash, cash equivalents, and restricted cash of $229,381 and $25,207 as of December 31, 2020 and 2019, respectively, based on Level 1 inputs.

The Company estimates the fair value of the warrant liability using the Black-Scholes option-pricing model at each balance sheet date or when specific events occur. As discussed in Note 13, in connection with the Company's IPO the warrant fair value was updated on August 19, 2020 with the change in fair value recorded in current period earnings as other expense in the consolidated statement of operations and reclassified to equity. During the year ended December 31, 2020, a loss of $3,109 was recorded in other expense in the consolidated statements of operations due to the change in the fair value of the warrant liability.

The range of assumptions used to determine the fair value of the warrant liability through August 19, 2020 were as follows:

Dividend yield	0.0%
Expected volatility	54.2% - 68.8%
Risk-free interest rate	0.17% - 1.56%
Lack of marketability discount	0.0%
Expected term (years)	1 - 4.5

17. RELATED-PARTY TRANSACTIONS

The Company was party to a management agreement for professional services provided by a related party, Paragon. The related party is an entity that shares common ownership with the Company. In addition, the Chairman of the Company's board of directors was the President and owner of the entity. For the year ended December 31, 2020 and 2019, respectively, the Company incurred $7,384 and $5,378, respectively, in management fee expense and other expenses to this related party, which are included in general and administrative expense in the consolidated statements of operations and comprehensive loss. The Company terminated the Management Services Agreement upon the consummation of its IPO. The Company is also party to a right of use agreement with the related party whereby it has access to and the right to use certain office space leased by the related party in Chicago, Illinois. In addition, the Company had participated in certain transactions with separate related parties that also share common ownership with the Company, primarily related to combined employee health plans. As of December 31, 2020 and 2019, respectively, the amounts due to related parties included in current liabilities were $0 and $1,208, respectively, and the amount included in other assets was $1 and $210, respectively.

18. SUBSEQUENT EVENTS

On January 6, 2021, the Company paid the $100,000 milestone payment to Bioprojet for the FDA approval of the NDA for WAKIX for the treatment of cataplexy in adult patients with narcolepsy.

In January and February 2021, the board of directors granted to various employees 882,606 employee stock options to purchase the Company's common stock. These awards were granted under the 2020 Plan and vest over a four-year period where 50% cliff vest after the second year and monthly thereafter.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our principal executive officer and principal financial officer have concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the Company's registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

Our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within our Company have been detected.

Item 9B. Other Information.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated by reference. The Proxy Statement will be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

Our board of directors has adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including our Chief Executive Officer, Chief Financial Officer and other executive and senior financial officers. The full text of our code of business conduct and ethics is posted on the investor relations page on our website which is located at https://ir.harmonybiosciences.com. We will post any amendments to our code of business conduct and ethics other than technical, administrative or other non-substantive amendments, or waivers of its requirements, on our website or in a Form 8-K filed with the SEC.

Item 11. Executive Compensation.

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated herein by reference. The Proxy Statement will be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated herein by reference. The Proxy Statement will be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated herein by reference. The Proxy Statement will be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in our Proxy Statement for the 2021 Annual Meeting of Stockholders and is incorporated herein by reference. The Proxy Statement will be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements

See "Part II—Item 8. Financial Statements and Supplementary Data.—Index to Financial Statements."

(a)(2) Financial Statement Schedules

All financial statement schedules have been omitted as the information is not required under the related instructions or is not applicable or because the information required is already included in the financial statements or the notes those financial statements.

(a)(3) Exhibits.

The documents set forth below are filed herewith or incorporated herein by reference to the location indicated.

EXHIBIT INDEX

Exhibit No.	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation of Harmony Biosciences Holdings, Inc.	8-K	August 21, 2020	3.1	
3.2	Amended and Restated Bylaws.	8-K	August 21, 2020	3.2	
4.1	Form of Common Stock Certificate.	S-1/A	August 6, 2020	4.1	
4.3	Description of Registrant's Securities.				X
10.1	Credit Agreement, dated as of January 9, 2020, among Harmony Biosciences, LLC, the Lenders from time to time party thereto and OrbiMed Royalty & Credit Opportunities III, LP.	S-1	July 27, 2020	10.1	
10.2	Pledge and Security Agreement, dated as of January 9, 2020, among Harmony Biosciences, LLC, the Registrant, OrbiMed Royalty & Credit Opportunities III, LP and the Secured Parties as defined therein.	S-1	July 27, 2020	10.2	
10.3	Harmony Biosciences Holdings, Inc. 2020 Incentive Award Plan	S-8	August 21, 2020	10.2	
10.4	Form of Option Agreement under Harmony Biosciences Holdings, Inc. 2020 Incentive Award Plan.	S-8	August 21, 2020	10.3	
10.5	Form of Restricted Stock Unit Agreement under Harmony Biosciences Holdings, Inc. 2020 Incentive Award Plan.	S-1/A	August 11, 2020	10.6	
10.6	Harmony Biosciences Holdings, Inc. 2020 Employee Stock Purchase Plan.	S-1/A	August 11, 2020	10.7	

10.7	Amended and Restated Employment Agreement, dated August 11, 2020, by and between Harmony Biosciences, LLC and John C. Jacobs.	S-1/A	August 11, 2020	10.8
10.8	Form of Indemnification Agreement between Harmony Biosciences, LLC and each director and executive officer.	S-1/A	August 11, 2020	10.12
10.9	Harmony Biosciences, LLC Separation Plan.	S-1/A	August 11, 2020	10.13
10.10	Harmony Biosciences Holdings, Inc. Amended and Restated 2017 Equity Incentive Plan.	S-1/A	August 11, 2020	10.3
10.11	Harmony Biosciences Holdings, Inc. Non-Employee Director Compensation Program.	10-Q	November 12, 2020	10.9
10.12	Offer Letter, dated October 10, 2017, by and between Harmony Biosciences, LLC and Jeffrey Dayno.	S-1/A	August 11, 2020	10.9
10.13	Offer Letter, dated September 8, 2017, by and between Harmony Biosciences, LLC and Andrew Serafin.	S-1/A	August 11, 2020	10.10
10.14	License and Commercialization Agreement, dated July 28, 2017, by and between Bioprojet Société Civile de Recherche and Harmony Biosciences, LLC.	S-1	July 27, 2020	10.10
10.15	Amendment No. 1 to License and Commercialization Agreement, dated August 27, 2018, by and between Bioprojet Société Civile de Recherche and Harmony Biosciences, LLC.	S-1	July 27, 2020	10.11
10.16	Trademark License Agreement, dated August 23, 2018, by and among Bioprojet Europe, Ltd., Bioprojet Société Civile de Recherche and Harmony Biosciences, LLC.	S-1	July 27, 2020	10.12
10.17	Management Services Agreement, dated September 22, 2017, by and between Paragon Biosciences, LLC and Harmony Biosciences, LLC.	S-1	July 27, 2020	10.13
10.18	Right of Use Agreement, dated November 1, 2019, by and between Paragon Biosciences, LLC and Harmony Biosciences, LLC.	S-1	July 27, 2020	10.14
10.19	Second Amended and Restated Investors' Rights Agreement, dated August 9, 2019, by and among the Registrant and the other parties thereto.	S-1	July 27, 2020	10.15

10.20	Offer Letter, dated September 7, 2017, by and between Harmony Biosciences, LLC and Jeffrey Dierks.				X
10.21	Confidential Separation Agreement and General Release, between Harmony Biosciences, LLC and Susan L. Drexler, dated March 4, 2021.	8-K		10.1	
10.22	Employment Agreement, dated March 4, 2021, between Harmony Biosciences, LLC and Sandip Kapadia.	8-K	March 15, 2021	10.1	
21.1	List of Subsidiaries of Harmony Biosciences Holdings, Inc.				X
23.1	Consent of Independent Registered Public Accounting Firm				X
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1**	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2**	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101	The following financial statements from the Company's Yearly Report on Form 10-K for the fiscal year ended December 31, 2020 formatted in Inline XBRL: (i) Balance Sheets, (ii) Statements of Operations, (iii) Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) and (vi) Notes to Financial Statements, tagged as blocks of text and including detailed tags.				X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)				X

* Indicates management contract or compensatory plan or arrangement.

** This certification is deemed furnished, and not filed, with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Harmony Biosciences Holdings, Inc. under the

Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

+ Certain portions of this document that constitute confidential information have been redacted in accordance with Regulation S-K, Item 601(b)(10)

Item 16. Form 10-K Summary.

None.

Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

HARMONY BIOSCIENCES HOLDINGS, INC.

By: /s/ John C. Jacobs
Name: John C. Jacobs
Title: President, Chief Executive Officer and Director

Date: March 25, 2021

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ John C. Jacobs John C. Jacobs	President, Chief Executive Officer, and Director (Principal Executive Officer)	March 25, 2021
/s/ Susan L. Drexler Susan L. Drexler	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 25, 2021
/s/ Jeffrey S. Aronin Jeffrey S. Aronin	Chairman of the Board	March 25, 2021
/s/ Antonio Gracias Antonio Gracias	Director	March 25, 2021
/s/ R. Mark Graf R. Mark Graf	Director	March 25, 2021
/s/ Eric Motley Eric Motley	Director	March 25, 2021
/s/ Jack Bech Nielsen Jack Bech Nielsen	Director	March 25, 2021
/s/ Juan A. Sabater Juan A. Sabater	Director	March 25, 2021
/s/ Gary Sender Gary Sender	Director	March 25, 2021
/s/ Andreas Wicki Andreas Wicki	Director	March 25, 2021

Exhibit 4.3

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following is a brief description of the capital stock of Harmony Biosciences Holdings, Inc. ("Company," "we," "us" or "our"). As of December 31, 2020, our common stock is the only class of our securities registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our amended and restated certificate of incorporation ("Certificate of Incorporation") and our amended and restated bylaws ("Bylaws"), each of which is filed as an exhibit to the Annual Report on Form 10-K of which this Exhibit [4.3] is a part, and the applicable provisions of the Delaware General Corporation Law ("DGCL"). We encourage you to read the Certificate of Incorporation, the Bylaws and the applicable provisions of the DGCL for additional information.

General

As of December 31, 2020, our authorized capital stock consisted of 500,000,000 shares of common stock, par value $0.00001 per share; and 10,000,000 shares of preferred stock, par value $0.00001 per share.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Upon our dissolution or liquidation, after payment in full of all amounts required to be paid to creditors and to the holders of preferred stock having liquidation preferences, if any, the holders of shares of our common stock will be entitled to receive pro rata our remaining assets available for distribution for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding.

Preferred Stock

Under the terms of our Certificate of Incorporation, our board of directors is authorized to provide for the issuance of up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

Forum Selection

Our Certificate of Incorporation provides that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will, to the fullest extent permitted by applicable law, be the sole and exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, other employees or stockholders to us or our stockholders; (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our Certificate of Incorporation or our Bylaws, or as to which the DGCL confers exclusive jurisdiction on the Court of Chancery; or (iv) any action asserting a claim governed by the internal affairs doctrine. Unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act or the Exchange Act. Any person or entity purchasing or otherwise acquiring or holding any interest in shares of our capital stock will be deemed to have notice of and consented to this provision.

Dividends

Declaration and payment of any dividend will be subject to the discretion of our board of directors. The time and amount of dividends will be dependent upon our business prospects, results of operations, financial condition, cash requirements and availability, debt repayment obligations, capital expenditure needs, contractual restrictions, covenants in the agreements governing our current and future indebtedness, industry trends, the provisions of Delaware law affecting the payment of distributions to stockholders and any other factors our board of directors may consider relevant. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business and to repay indebtedness, and therefore do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. Consequently, any gains from an investment in our common stock will likely depend on whether the price of our common stock increases.

Anti-Takeover Provisions

Our Certificate of Incorporation and Bylaws contain provisions that may delay, defer or discourage wanother party from acquiring control of us. We expect that these provisions, which

are summarized below, will discourage coercive takeover practices or inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors, which we believe may result in an improvement of the terms of any such acquisition in favor of our stockholders. However, they also give our board of directors the power to discourage acquisitions that some stockholders may favor.

Authorized but Unissued Shares

The authorized but unissued shares of our common stock and our preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of Nasdaq. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Classified Board of Directors

Our Certificate of Incorporation provides that our board of directors will be divided into three classes, with the classes as nearly equal in number as possible and each class serving three-year staggered terms. In all other cases and at any other time, directors may only be removed from our board of directors for cause by the affirmative vote of a majority of the shares entitled to vote. These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control of us or our management.

Stockholder Action; Special Meeting of Stockholders

Our Certificate of Incorporation provides that our stockholders will not be able to take action by written consent for any matter and may only take action at annual or special meetings. As a result, a holder controlling a majority of our capital stock would not be able to amend our Bylaws or remove directors without holding a meeting of our stockholders called in accordance with Bylaws, unless previously approved by our board of directors. Our Certificate of Incorporation further provides that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer, our president or another officer selected by a majority of our board of directors, thus limiting the ability of a stockholder to call a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

Advance Notice Requirements for Stockholder Proposals and Director Nominations

In addition, our Bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. In order for any matter to be “properly brought” before a meeting, a stockholder must comply with advance notice and duration of ownership requirements and provide us with certain information. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a qualified stockholder of record on

the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying stockholder actions that are favored by the holders of a majority of our outstanding voting securities until the next stockholder meeting.

Amendment of Certificate of Incorporation or Bylaws

The DGCL provides generally that the affirmative vote of the holders of a majority in voting power of the shares entitled to vote is required to amend a corporation's certificate of incorporation, unless a corporation's certificate of incorporation requires a greater percentage. Upon consummation of this offering, our Bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders a majority of the votes which all our stockholders would be eligible to cast in an election of directors.

Section 203 of the DGCL

We are subject to Section 203 of the DGCL, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Limitations on Liability and Indemnification of Officers and Directors

Our Bylaws provide indemnification for our directors and officers to the fullest extent permitted by the DGCL, along with the right to have expenses incurred in defending proceedings paid in advance of their final disposition. We have entered into indemnification agreements with each of our directors and executive officers that may, in some cases, be broader than the specific indemnification and advancement provisions contained under our Bylaws and provided under Delaware law. In addition, as permitted by Delaware law, our Certificate of Incorporation includes provisions that eliminate the personal liability of our directors for monetary damages resulting from breaches of certain fiduciary duties as a director. The effect of this provision is to restrict our rights and the rights of our stockholders to recover monetary damages against a director for breach of fiduciary duties as a director.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

Dissenters' Rights of Appraisal and Payment

Under the DGCL, with certain exceptions, our stockholders will have appraisal rights in connection with a merger or consolidation of Harmony Biosciences Holdings, Inc. Pursuant to the DGCL, stockholders who properly demand and perfect appraisal rights in connection with such mergers or consolidations will have the right to receive payment of the fair value of their shares as determined by the Delaware Court of Chancery, subject to certain limitations.

Stockholders' Derivative Actions

Under the DGCL, any of our stockholders may bring an action in our name to procure a judgment in our favor, also known as a derivative action, in certain circumstances. Among other things, either the stockholder bringing any such action must be a holder of our shares at the time of the transaction to which the action relates or such stockholder's stock must have thereafter devolved by operation of law, and such stockholder must continuously hold shares through the resolution of such action.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Trading Symbol and Market

Our common stock is listed on the Nasdaq Global Market under the symbol "HRMY."

Exhibit10.20

September 7th , 2017

Jeffrey Dierks
428 W. 5th Avenue
Conshohocken, PA 19428

Dear Jeff:

On behalf of Harmony Biosciences, LLC ("Harmony Biosciences" or the "Company"), I am pleased to extend an offer of employment with the Company as Vice President, Marketing. Except for business travel on behalf of the Company, you will work out of the Company's Philadelphia Regional Office and other Company venues. This position will report to the Chief Commercial Officer or his designee.

Your start date will be mutually determined but we anticipate it to be on or around October 2, 2017. We are excited about the possibility of you joining our team at Harmony Biosciences and hope you will accept our offer to join us in executing our growth plans for the Company.

The terms of your employment offer are outlined below:

- Bi-monthly base pay of $10,417 which, when annualized, is equivalent to a base salary of $250,000 per year.
- Participation (pro-rated for the calendar year in which your actual start date occurs) in the Harmony Biosciences, LLC Performance Bonus Plan at up to 35% of your base salary based on Company and individual achievement. Your bonus will be based on your performance meeting established individual goals and objectives to support the growth strategy of the Company, as well as the Company's overall performance.
- Equity in the Company's parent company, Harmony Biosciences II, Inc. ("Parent") 400,000 stock options for Parent common stock at an exercise price equal to the greater of $1.00 and the fair market value per share of common stock as of your start date, to be determined by the Parent's Board of Directors or its Compensation Committee, if applicable.
- As a full-time Company employee, you will accrue paid vacation and sick leave. Vacation will accrue at a rate of 1.25 days per month, or 15 days per year.
- In consideration of the money left behind at your current employer for 2017 pro-rated annual bonus and LTI, you will receive a sign-on bonus of $100,000 (subject to applicable tax and other withholding), paid to you in two installments. The first will be 50% ($50,000) and paid no later than 12/31/2017. The second will be 50% ($50,000) and paid on 12/31/2018. Both payments require that you are an active employee in good standing at the time of payment. If you leave the company for any reason within 12 months after receiving the first payment or 6 months after receiving the second sign-on bonus payments, you must pay back the full pre-tax amount of that payment to Harmony Biosciences.

- This offer is contingent upon successful completion of Harmony's pre-employment process.

You will devote all of your time and attention to the Company (including, but not limited to, its business, operations and success) and shall not compete with the Company in any way during your employment.

As a full-time employee of the Company, except as expressly provided for above, you are eligible to participate in the provided Harmony Biosciences, LLC Employee Benefit Plans.

This offer of employment, if not previously accepted by you, will expire ten days after the date first set forth above. This offer of employment does not represent an employment contract. Just as you retain the right to resign, with or without notice or cause, Harmony Biosciences has the same right with respect to termination of your employment. You will be an employee at will, and your employment is for no definite term, regardless of any other oral or written statement by any Harmony Biosciences officer or representative, with the exception of an express written employment contract signed by the CEO, President or Chief Legal Officer of the Company. Notwithstanding anything in this offer of employment to the contrary, if your actual start date does not occur on or prior to October 2, 2017, this offer of employment will be null and void in its entirety (even if previously accepted by you).

If you understand and accept these terms, please sign and return one copy of this offer letter to me. We would love to have you join Harmony Biosciences and be a part of building a great company. Should you have any questions regarding this offer, please feel free to contact me at 847-715-0611.

Sincerely,

/s/ Anna Fenkanyn

Anna Fenkanyn
Human Resources

Agreed to and Accepted by:

/s/ Jeffrey Dierks	9/9/17
Jeffrey Dierks	Date

Exhibit 21.1

Subsidiaries of Harmony Biosciences Holdings, Inc.

Subsidiary	Jurisdiction
Harmony Biosciences, LLC	Delaware

US-DOCS\121964576.1

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-248243 on Form S-8 of our report dated March 25, 2021, relating to the financial statements of Harmony Biosciences Holdings, Inc. appearing in this Annual Report on Form 10-K of Harmony Biosciences Holdings, Inc. for the year ended December 31, 2020.

/s/ DELOITTE & TOUCHE LLP

Chicago, Illinois
March 25, 2021

Exhibit 31.1

Certification of Principal Executive Officer

I, John C. Jacobs, certify that:

1. I have reviewed this Annual Report on Form 10-K of Harmony Biosciences Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 25, 2021

By: /s/ John C. Jacobs

Name: John C. Jacobs

Title: President and Chief Executive Officer (Principal Executive Officer)

Exhibit 31.2

Certification of Principal Financial Officer

I, Susan L. Drexler, certify that:

1. I have reviewed this Annual Report on Form 10-K of Harmony Biosciences Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 25, 2021

By: /s/ Susan L. Drexler

Name: Susan L. Drexler

Title: Chief Financial Officer and Treasurer (Principal Financial Officer)

Exhibit 32.1

Certification of Principal Executive Officer
Pursuant To 18 U.S.C. Section 1350,
as Adopted Pursuant to
Section 906 of The Sarbanes-Oxley Act of 2002

In connection with the Annual Report on Form 10-K of Harmony Biosciences Holdings, Inc. (the "Company") for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to such officer's knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 25, 2021

By: /s/ John C. Jacobs

Name: John C. Jacobs

Title: President and Chief Executive Officer (Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as a part of the Report or on a separate disclosure document.

Exhibit 32.2

Certification of Principal Financial Officer
Pursuant To 18 U.S.C. Section 1350,
as Adopted Pursuant to
Section 906 of The Sarbanes-Oxley Act of 2002

In connection with the Annual Report on Form 10-K of Harmony Biosciences Holdings, Inc. (the "Company") for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to such officer's knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 25, 2021

By: /s/ Susan L. Drexler

Name: Susan L. Drexler

Title: Chief Financial Officer and Treasurer (Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as a part of the Report or on a separate disclosure document.