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 EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

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 001-40353

IMPEL PHARMACEUTICALS INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**26-3058238**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
201 Elliott Avenue West, Suite 260, Seattle, WA	**98119**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (206) 568-1466

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 $0.001 per share	IMPL	The Nasdaq Stock 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 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, smaller reporting company, or an emerging growth company. See the 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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant on June 30, 2022 (the last business day of the Registrant's second fiscal quarter), based upon the closing price of $9.32 of the Registrant's common stock as reported on The Nasdaq Global Market, was approximately $119.7 million.

The number of shares of Registrant's Common Stock outstanding as of March 15, 2023 was 23,746,257.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, in connection with the registrant's 2023 Annual Meeting of Stockholders (the "2023 Proxy Statement").

Table of Contents

PART 1

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. This section should be read in conjunction with our audited consolidated financial statements and related notes included in Part II, Item 8 of this report. The statements contained in this report that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended.

In some cases, you can identify forward-looking statements by such terminology as "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" and similar expressions that convey uncertainty of future events or outcomes, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements about:

- our ability to successfully execute our commercialization strategy for Trudhesa;
- our expectations regarding our plans to pursue a new strategic reprioritization, halt research and development on certain product candidates, and the associated cost savings;
- the size and growth potential of the market for Trudhesa and the markets for any future product candidates, if approved for commercial use, and our ability to serve those markets;
- our ability to obtain and maintain regulatory approval of any future product candidates, and any related restrictions, limitations or warnings in the label of any approved product;
- the timing or likelihood of regulatory filings and approvals;
- the success, cost and timing of our development activities, preclinical studies and clinical trials;
- the number, size and design of clinical trials that regulatory authorities may require to obtain marketing approval;
- our plans relating to the future development and manufacturing of product candidates, including plans for future development of our POD devices and proprietary POD technology, and plans to address additional indications for which we may pursue regulatory approval;
- future agreements with third parties in connection with preclinical and clinical development as well as the manufacture and commercialization of product candidates, if approved for commercial use;
- our ability to attract customers for any approved products;
- the effect of litigation, complaints or adverse publicity on our business;
- our ability to expand our sales force to address effectively the new indications, geographies and types of organizations we intend to target;
- our ability to forecast and maintain an adequate rate of revenue growth and appropriately plan our expenses;
- our liquidity and working capital requirements;
- our ability to attract and retain qualified employees and key personnel;
- our ability to protect and enhance our brand and intellectual property;
- the costs related to defending intellectual property infringement and other claims;
- privacy, data security, and data protection laws, actual or perceived privacy or data breaches or other data security incidents, or the loss of data;
- future regulatory, judicial, and legislative changes in our industry;
- future arrangements with, or investments in, other entities or associations, products, services or technologies;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and the increased expenses and administrative workload associated with being a public company.

These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part I, Item 1A — "Risk Factors," and elsewhere in this report. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. In this report, "we," "our," "us," "Impel," and "the Company" refer to Impel Pharmaceuticals Inc.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

The marks "IMPEL," "POD," "TRUDHESA," "IMPELPOD," the Impel Logo, the Impel Dots Logo, the Trudhesa Logo, and our other registered or common law trade names, trademarks or service marks appearing in this report are the property of Impel. All other service marks, trademarks and trade names appearing in this report are the property of their respective owners.

PART I

Item 1. Business.

Overview

We are a commercial-stage biopharmaceutical company with a mission to develop transformative therapies for people suffering from diseases with high unmet medical needs, with an initial focus on the Central Nervous System, or CNS. Our company was founded on the premise that the upper nasal space can be an optimal treatment entry point for CNS and other diseases where rapid vascular absorption can result in superior clinical outcomes. Our strategy is to pair our proprietary POD upper nasal delivery technology with well-established therapeutics or other therapeutics where rapid vascular absorption is preferred to drive therapeutic benefit, improve patient outcomes, reduce drug development risk and expand the commercial opportunity within our target diseases. On September 2, 2021, the U.S. Food and Drug Administration, or FDA approved our New Drug Application, or NDA for Trudhesa for the acute treatment of migraine headaches with or without aura in adult patients. We launched Trudhesa in early October 2021. Since 2016, we have identified and advanced several product candidates, including INP105 for the acute treatment of agitation and aggression in patients with autism spectrum disorder, or ASD. On February 22, 2023, we announced plans to reduce our workforce by approximately 16% primarily impacting the research and development functions. These actions reflects our determination to refocus our strategic priorities around Trudhesa and will halt research and development efforts on INP105.

We have designed our proprietary POD technology to target the vascular-rich upper nasal space, and to provide rapid absorption, consistent drug biodistribution and ease of use for a patient, provider or caregiver. Our goal with our POD technology is to deliver injection-like clinical outcomes non-invasively. We believe that we are the first company to successfully harness the benefits of delivery to the upper nasal space to improve delivery and the pharmacologic potential of CNS therapies.

POD Technology

Using our proprietary POD technology, we have developed devices that deliver therapeutics directly to the upper nasal space. These devices are designed to offer several key benefits compared to traditional nasal delivery systems, including:

- ***Rapid Onset.*** The precise spray plume and biphasic nature of delivery to the upper nasal space allows for superior dose deposition and rapid absorption into the systemic circulation as compared to traditional nasal delivery systems.
- ***Consistent Drug Bioavailability***. Metered propellant dosing allows for more consistent blood levels than typically seen with traditional nasal sprays and are equivalent, or superior, to those achieved through intramuscular, or IM, injections.

- ***Improved Patient-Provider Experience***. Our proprietary gas propulsion mechanism eliminates the need for coordination of breathing and enables delivery of a dosing in 1/10th of a second, enabling self- or provider-administration in a manner that improves patient comfort and compliance.
- ***Manufacturability***. Separation of propellant and drug within the POD device helps streamline the development of chemistry, manufacturing, and controls, or CMC, development, as we are not constrained by the limits of co-formulating our therapeutics inside a pressurized propellant canister.
- ***Formulation Versatility***. The POD device is versatile and can deliver both liquid and powder formulations in order to potentially address a wide variety of indications across multiple therapeutic areas.
- ***Strong Intellectual Property Position***. We believe that we have a strong global intellectual property position relating to Trudhesa and our prior product candidates. Our patent portfolio as of February 1, 2023, contained 14 U.S. issued patents and 74 patents issued in ex-U.S. jurisdictions related to Trudhesa, our POD technology, and combination products in development. We also have 13 U.S. pending applications as well as 67 patent applications pending in ex-U.S. jurisdictions. Our patent portfolio is expected to provide patent protection ranging from 2032 to 2040.

We believe that our expertise positions us to address unmet medical needs across multiple therapeutic areas by delivering well-established and novel drugs consistently, rapidly and non-invasively. In addition to our technology and development expertise, our strong intellectual property portfolio protects multiple aspects of our approach to delivering drug to the upper nasal space. We believe that our apparatus, composition of matter and method of use intellectual property can provide strong exclusivity protection to our prior product candidates.

Marketed Product

Trudhesa (Acute Treatment of Migraine)

Trudhesa (formerly known as INP104) is a liquid formulation of dihydroergotamine, or DHE, administered to the upper nasal space using our proprietary POD technology for the acute treatment of migraine headaches with or without aura in adults. The migraine market is projected to grow at a compound annual growth rate or CAGR, of 9.9% reaching $12 billion by 2030 with the introduction of multiple new product offerings and an expected increase in disease awareness and diagnosis. DHE is widely used as part of a standard of care for treatment of migraines, despite being limited to IV and injection delivery or traditional nasal administration. IV delivery requires administration in physicians' offices, migraine clinics and hospitals, and traditional nasal administration has been challenged by inconsistent efficacy.

In June 2020, we announced the following exploratory efficacy results of our STOP301 trial to evaluate the safety and tolerability of long-term, intermittent use of Trudhesa as an acute treatment of migraine with or without aura in adult patients. In this trial, baseline results prior to trial initiation were based on migraine attacks where patients used their standard acute migraine medication. In the trial:

- 38% of patients were pain free at two hours after their first dose of Trudhesa.
- 52% of patients receiving Trudhesa were free of their most bothersome migraine symptom at two hours.
- Patients treated with Trudhesa also demonstrated improvement in pain relief: 16% of patients treated with Trudhesa had pain relief within 15 minutes of treatment, and 66% had pain relief within two hours.

The exploratory endpoints of the trial also included an assessment of the following long-term outcomes of Trudhesa when patients were treated for six months:

- 39% of patients treated with Trudhesa remained pain free at two hours through three months of treatment and 35% of patients treated with Trudhesa remained pain free at two hours through six months of treatment.
- Patients who received Trudhesa saw a 48% reduction in the frequency of their migraines compared to baseline during the 24-week trial.
- 93% and 86% of patients achieving pain freedom at two hours after their first dose of Trudhesa did not suffer a relapse in migraine or require a rescue medication at 24 hours and 48 hours, respectively.
- Health economic data showed a meaningful reduction in the usage of healthcare resources by patients treated with Trudhesa versus their baseline. Emergency room visits were reduced by approximately 73% and hospitalizations and urgent care visits were reduced by 100%.

Although the trial was not powered to determine statistical significance of the exploratory efficacy endpoints, we believe these exploratory endpoints provide important data for evaluating the clinical benefit of Trudhesa and showed consistency with the generally understood benefits of DHE for the acute treatment of migraines. The primary endpoints of the STOP 301 trial were safety and tolerability of long-term, intermittent use. In this trial, Trudhesa was generally well tolerated. There were a total of seven treatment emergent serious adverse events, or SAEs, none of which were determined by the investigator to be related to Trudhesa or led to withdrawal from the trial. There were also no significant changes to sense of smell, and no significant abnormal findings from nasal endoscopy examinations.

In November 2020, we submitted an NDA for Trudhesa for the acute treatment of migraine headaches with or without aura in adult patients. On September 2, 2021, the FDA approved our NDA for Trudhesa for the acute treatment of migraine headaches with or without aura in adult patients.

Given the concentrated prescriber base of our target market for Trudhesa, we independently launched in October 2021. Trudhesa was launched with an initial sales force of 60 representatives and was recently expanded to approximately 90 representatives to support our targeted launch strategy. The current listed wholesale acquisition price, or WAC, price of Trudhesa is $892.50 for four doses (1pack). Through December 31, 2022, there have been approximately 58,420 prescriptions of Trudhesa generated since launch and, based on third-party data, we believe Trudhesa accounts for approximately 4.3% of total branded acute migraine prescriptions among over 2,000 unique Trudhesa prescribers since launch. Additionally, based on internal data, approximately 63% of new Trudhesa patients eligible for a refill have received a second prescription. The sales team is supported by an established market access, medical affairs, marketing, and operations infrastructure. Our commercial efforts are focused on approximately 11,000 high value healthcare professional or HCP, targets that prescribe approximately 40% of all migraine prescriptions and 73% of all acute branded prescriptions. Importantly, we have secured managed care contracts providing access to Trudhesa for approximately 80% of commercial lives in the United States. We have deployed a robust sample program to ensure trial with Trudhesa for patients seeking better treatments and outcomes. Through both our commercial and medical affairs infrastructure we have engaged healthcare practitioners and patients, partnered with national associations and actively supported advocacy groups in the migraine market. These efforts have been, and will continue to be, supplemented with non-personal promotion to all targeted and non-targeted medium value physicians. To capture the maximum commercial opportunity of Trudhesa, we may also selectively seek partners to commercialize the product outside of our target markets, including additional penetration within the broader primary care setting, as well as in geographies outside of the United States.

Our Team

We have assembled a team of scientific and business leaders with deep expertise in neuroscience and a track record of building, growing and commercializing new products. Our Chairman and Chief Executive Officer, Adrian Adams, has over 25 years of pharmaceutical experience with an emphasis on commercialization and strategic execution. Our co-founder and Chief Technology and Development Officer, John Hoekman, Ph.D., has over 15 years of experience in investigating upper nasal drug delivery and nose-to -brain delivery, is an inventor of our proprietary POD technology, is widely recognized as a pioneer in upper nasal space drug delivery and has evaluated over 30 CNS targeting compounds with over six different modalities including small molecules, proteins, peptides and antibodies as opportunities for upper nasal space delivery. Our Chief Commercial Officer, Leonard S. Paolillo, has nearly 20 years of experience with various companies in the healthcare and pharmaceutical industries, including Warner Chilcott and Kyowa Kirin. We are supported by our board of directors, scientific advisory boards and a group of leading biotechnology-focused investors, including KKR Iris, Norwest Venture Partners, 5AM Venture Management, LLC, venBio and Vivo Capital.

Our Strategy

Our goal is to deliver transformative therapies, harnessing the benefits of delivery to the upper nasal space, to patients suffering from CNS diseases and other diseases with high unmet medical needs. The key tenet of our strategy to accomplish this goal include:

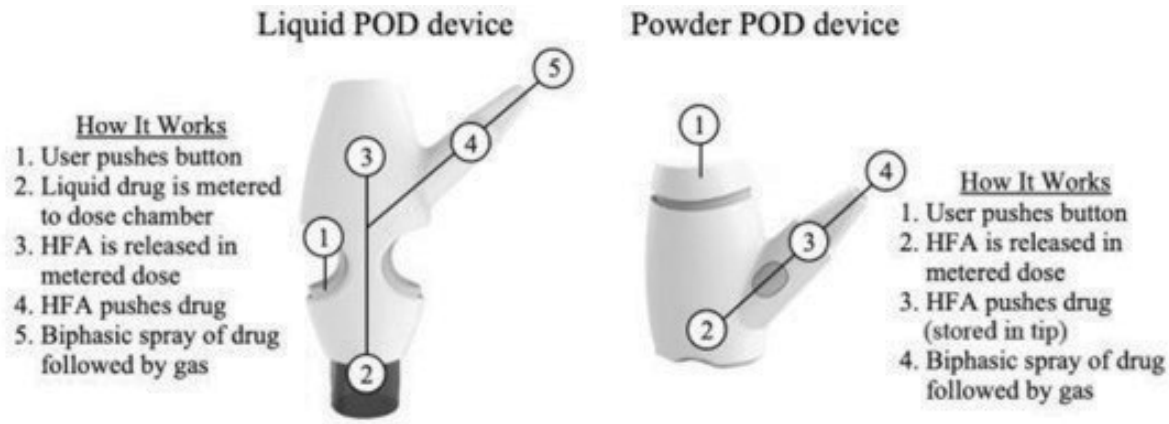
- ***Successfully commercialize Trudhesa for the acute treatment of migraine***. Given the concentrated prescriber base of our target market for Trudhesa, we independently launched in October 2021. Trudhesa was launched with an initial sales force of 60 representatives and was recently expanded to approximately 90 representatives to support our targeted launch strategy. The current listed WAC price of Trudhesa is $892.50 for four doses (1pack). Through December 31, 2022, there have been approximately 58,420 prescriptions of Trudhesa generated since launch and, based on third-party data, we believe Trudhesa accounts for approximately 4.3% of total branded acute migraine prescriptions among over 2,000 unique Trudhesa prescribers since launch. Additionally, based on internal data, approximately 63% of new Trudhesa patients eligible for a refill have received a second prescription. The sales team is supported by an established market access, medical affairs, marketing, and operations infrastructure. Our commercial efforts are focused on approximately 11,000 high value HCP targets that prescribe approximately 40% of all migraine total prescriptions

and 73% of all acute branded total prescriptions. Importantly, we have secured managed care contracts providing access to Trudhesa for approximately 80% of commercial lives in the United States. We have deployed a robust sample program to ensure trial with Trudhesa for patients seeking better treatments and outcomes. Through both our commercial and medical affairs infrastructure we have engaged healthcare practitioners and patients, partnered with national associations and actively supported advocacy groups in the migraine market. These efforts have been, and will continue to be, supplemented with non-personal promotion to all targeted and non-targeted medium value physicians. To capture the maximum commercial opportunity of Trudhesa, we may also selectively seek partners to commercialize the product outside of our target markets, including additional penetration within the broader primary care setting, as well as in geographies outside of the United States.

- ***Maximize the therapeutic and commercial potential of our proprietary POD technology platform through selective partnerships***. Based on the unique characteristics and versatility of our proprietary POD technology, we believe we are positioned to partner with other firms to address multiple therapeutic areas with unmet medical needs. While our initial focus is to address CNS diseases, we intend to explore the broader therapeutic utility of our POD technology in diseases where rapid vascular absorption can result in superior clinical outcomes. In doing so, we may elect to enter into collaborations for third-party product candidates for which we believe that our technologies and expertise may be valuable.

Our Technology

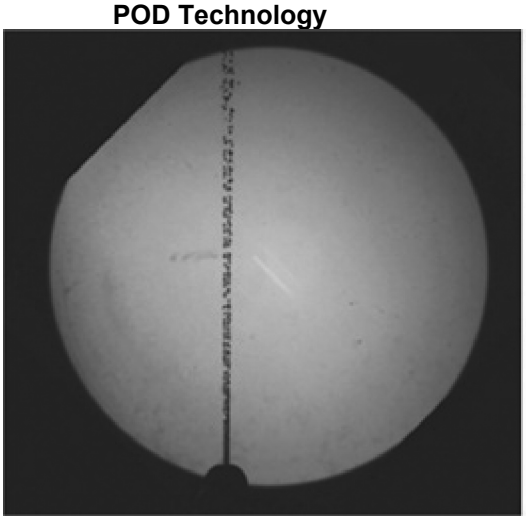
We have developed upper nasal space devices to enable differentiated clinical profiles for any prior or future product candidates. These devices utilize our proprietary POD technology propellant and a biphasic spray that creates a precise plume or stream of drug to initially reach the vascular-rich upper nasal space and then a second puff of propellant to further distribute drug across the upper nasal space. Two of our devices are depicted below.



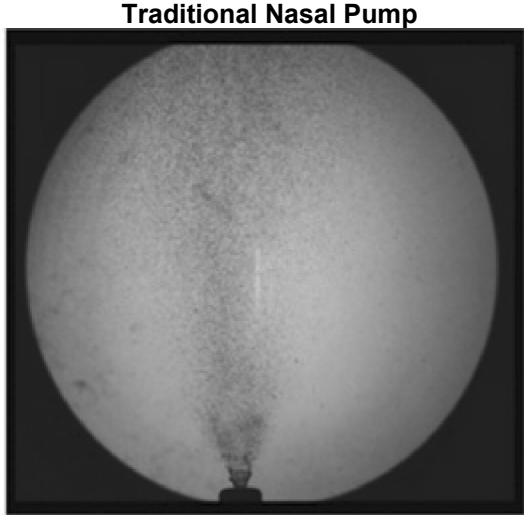
We have designed our proprietary POD technology to target the vascular-rich upper nasal space, and to provide rapid absorption, consistent drug biodistribution and ease of use for a patient, provider or caregiver. Our goal with our POD technology is to deliver injection-like clinical outcomes non-invasively. We believe that we are the first company to successfully harness the benefits of delivery to the upper nasal space to improve the therapeutic potential of CNS therapies. Traditional nasal pumps have suffered from high variability and low overall absorption. These characteristics have generally limited the nasal route of administration to local treatment of allergies or nasal inflammation. We have pioneered research into systemic drug delivery through the upper nasal spacey, the anatomy of which is depicted in the picture below, to the CNS. We have demonstrated with multiple molecules that targeting the upper nasal space could improve the bioavailability and biodistribution of drugs into the systemic circulation. The upper nasal space is more permeable, has a higher density of vasculature and has a reduced clearance rate compared to the lower nasal space. These advantages of the upper nasal space may allow for a better consistency in dosing and uptake as well as the potential for faster time to onset of action. We have spent years developing device technologies and drug formulations to take advantage of this route of administration. We currently pair our technologies with established therapeutics approved through other routes of administration to create drug-device combination product candidates with the potential to address significant unmet medical needs and broaden the addressable patient population within our initial indications. This technology also offers potential to expand into other therapeutic areas.

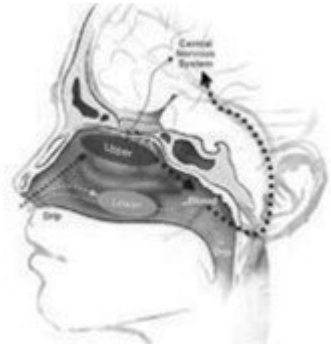
As demonstrated in the figures below, compared to traditional nasal pumps, which have a diffuse aerosol spray, the POD technology creates a soft focused stream which consistently delivers drug to the upper nasal space. The figure on the top left shows a demonstrative spray pattern of DHE in our proprietary POD technology. The figure on the top right shows a demonstrative spray pattern of DHE in a traditional nasal pump. The figure on the bottom left shows the different route to the CNS as a result of upper nasal space delivery.

POD Technology



Traditional Nasal Pump





Potential Advantages of Upper Nasal Space Delivery

- Rapid uptake into the blood stream
- Decreased dripping and swallowing
- Consistent dosing and distribution

Our proprietary POD technology is designed to offer a number of key benefits compared to traditional nasal delivery systems. These features include:

- ***Dose Consistency***. Consistent dosing is critical to producing predictable and reproducible clinical outcomes. Unlike existing nasal delivery systems, which rely solely on mechanical pressure to deliver the drug into the nasal space, our proprietary POD technology utilizes hydrofluoroalkane, or HFA, gas as a propellant to expel the drug from our device into the upper nasal space, allowing us to achieve dose consistency within a 15% standard deviation of the mean consistent with guidance from the FDA.
- ***Biphasic Spray***. The POD devices deliver drugs through a biphasic spray, which consists of a first phase that delivers the drug to the upper nasal space and then a second phase that further distributes the drug across the mucosa of the upper nasal space.
- ***Narrow Plume Geometry***. Traditional nasal delivery systems create a wide aerosol plume that is typically unable to get through the two-to-three millimeter wide nasal valve and into the upper nasal space, which creates variability in the absorption of the drug. The POD devices use a proprietary drug flow path and nozzle to create a narrow spray plume that can deliver drug past the nasal valve and into the upper nasal space.
- ***Reduces Human Error***. Conventional nasal spray devices rely on the user to breathe in through their nasal passages while the dose is being administered. This can be challenging for patients to perform synchronously and consistently. The POD device uses HFA gas to expel drug into the upper nasal space. The HFA gas is metered out in a consistent manner regardless of how much force the user applies to actuate the device. The HFA gas is then able to consistently expel the drug with less chance for user error. These features allow the POD devices to be used independently of patients' breathing coordination, which may lead to more consistent drug absorption.

- ***Separated Drug and Propellant***. In product candidates, the drug formulation and propellant are maintained in separated compartments of the device until delivery of the dose. This separation of the drug and propellant allows us to formulate product candidates without being constrained by the limits of formulating inside a pressurized propellant canister. We are developing POD devices for both liquid and powder drug formulations, and we believe that these devices can deliver a wide range of total dose.

We have developed unique POD devices for each of nonclinical development, early clinical trials, pivotal studies and commercialization. We have spent years developing these nonclinical devices and methods to create a robust early development process. With our historical product candidates, we have done extensive nonclinical testing to assess safety and expected clinical performance. Our proprietary POD technology allows for rapid decision making when advancing product candidates into clinical development by testing a variety of doses and formulations. With our proprietary POD technology, we have evaluated in a nonclinical setting multiple additional candidates that could be developed further in the future.

In addition to our proprietary POD technology, we have expertise in developing proprietary upper nasal formulations that further improve the product profile. The flexibility of our proprietary POD technology to deliver both liquid and powder formulations allows us to develop the most appropriate formulation for the patient, indication and dosing regimen. We evaluate each molecule in early development with the goal of making the simplest robust formulation using inactive ingredients present in FDA-approved drug products. Our proprietary POD technology is not reliant on breath coordination and our nasal drug formulations do not need to achieve a specific particle size range like pulmonary delivery products, which allows for more flexibility in the manufacturing process. Our expertise in upper nasal formulation allows us to select therapeutics that are already in wide use and regarded as safe in other delivery formats for our product candidate pipeline. We believe we can also pair our proprietary POD technology with new chemical entities.

We believe that we have the ability to use our proprietary POD technology and upper nasal formulation expertise to produce product candidates that allow for convenient, non-invasive administration with the potential for injection-like clinical outcomes. Given their ease of administration, product candidates can be self- or caregiver-administered outside of traditional patient care settings, thus expanding patient access. Additionally, our separation of propellant and drug in the POD device allows for reduced CMC risks. The unique characteristics of certain product candidates may have the potential to address unmet needs across multiple CNS diseases.

We have issued patent claims covering certain devices and methods of drug delivery, as well as pending patent applications directed to certain other embodiments of our device, drug formulations and methods of using our historical product candidates. We believe that this apparatus, composition of matter and method of use intellectual property can provide strong exclusivity protection to our historical product candidates. Our existing solely owned patent portfolio is expected to provide patent protection ranging from 2032 to 2040, unless we receive patent term adjustment or patent term extension, or both.

Marketed Product

Trudhesa for the Acute Treatment of Migraine

Trudhesa is a liquid formulation of DHE administered using our proprietary POD technology to the upper nasal space for the acute treatment of migraine headaches with or without aura in adult patients. Trudhesa was previously known as INP104. DHE is widely used as part of a standard of care for the acute treatment of migraines but is generally limited to IV and injection delivery administered in physicians' offices, migraine clinics and hospitals, or nasal delivery to the lower nasal space. In June 2020, we announced positive results from our 360-patient STOP 301 trial to evaluate the safety and tolerability of long-term, intermittent use of Trudhesa, and in November 2020, we submitted an NDA for Trudhesa for the acute treatment of migraine headaches with or without aura in adult patients. On September 2, 2021, the FDA approved our NDA for Trudhesa. Trudhesa is not indicated for the preventive treatment of migraine or the management of hemiplegic or basilar migraine.

Disease Overview and Market Opportunity

Migraine is a chronic and debilitating disorder characterized by recurrent attacks generally lasting four to 72 hours with multiple symptoms, including typically one-sided, pulsating headaches of moderate to severe pain intensity that are associated with nausea or vomiting, sound sensitivity, smell sensitivity and light sensitivity. Migraines are often preceded by transient neurological warning symptoms, known as auras, which typically involve visual disturbances such as flashing lights but may also involve numbness or tingling in parts of the body. Migraines are both widespread and disabling.

The State of U.S. Health, 1990-2016 Study rates migraine as the fifth leading cause of years lived with disability in 2016. Based on market research commissioned by us, we believe that approximately 31 million individuals in the United

States suffer from migraine attacks. Most sufferers experience migraine attacks once or twice per month and over 1.2 million emergency room visits per year are for acute treatment of migraine attacks. The migraine market is projected to grow at a CAGR of 9.9% reaching $12 billion by 2030 with the introduction of multiple new product offerings and an expected rise in disease awareness and diagnosis. Additionally, with the approvals of monoclonal antibodies against calcitonin gene-related peptide for migraine prevention and the approvals of new therapies for the acute treatment of migraine, such as oral gepants and lasmiditan, the awareness of migraine and its impact, and treatment options are expected to continue to grow. Of the approximately 18 million diagnosed migraine patients, approximately 12 million are not on active treatment. Of the six million patients diagnosed and on prescription treatment, up to 79% of the patients are willing to try another medication for the acute treatment of migraine. Further, in a 2017 survey of nearly 4,000 U.S. patients using oral acute prescription medication for migraine, 96% said they were dissatisfied with at least one aspect of their treatment, 48% said they can still have pain two hours after taking medication and 38% said their headache returns within 24 hours of getting relief.

Acute Treatment of Migraine and Limitation of Other Approved Treatments

Until the recent approval of the gepants and lasmiditan drugs, there has been limited innovation in the acute treatment of migraine since the introduction of triptans in 1992. Additional pharmacologic agents used for the acute treatment of migraine include analgesics, non-steroidal anti-inflammatory drugs, anti-emetics and ergots. The migraine market has steadily increased from approximately 20 million prescriptions in 2017 to approximately 33 million prescriptions in 2022, while triptans' share of the migraine market has steadily decreased from approximately 97% in 2017 to 69% in 2022. While triptans remain the most common prescribed therapy for migraines, they possess four major limitations that result in an unmet need for migraine patients:

- *Unmet Need for Efficacy*. Approximately 30% to 40% of migraine patients do not fully respond to triptans, and alternatives, including gepant and lasmiditan drugs, are limited. Triptans have also been shown to be more efficacious when taken early in a migraine attack, but those patients who wait or delay treatment may not experience the full benefit of triptan therapy.
- *Need for More Rapid Onset*. While triptans have improved the treatment of migraine, their onset of pain relief is relatively slow. Historically, estimated onset of significant pain relief with oral triptans occurs between one and three hours after dosing.
- *Need for Longer Duration of Effect*. Published studies cite that the recurrence within 24 hours of an effectively treated migraine is a common reason given for dissatisfaction with triptans.
- *Opportunity for Improved Tolerability Profile*. Triptans can be associated with the following side effects: dizziness, dry mouth, feeling heavy in one's face, arms, legs, and chest, feeling sleepy, flushing, muscle weakness and nausea.

The recent approvals of gepant and ditan drugs have introduced new migraine treatment options into the market. While these oral medications are generally an improvement over triptans, there remains a significant unmet need. As oral medications, these products have relatively low efficacy and persistence rates. Further, ditans have significant potential side effects, including potential driving impairment, sleepiness and dizziness. In a recent survey of neurologists and headache specialists, a substantial majority of surveyed physicians agreed that the association between migraine and gastrointestinal disorders is important in the acute treatment of migraine, as it may result in lowered efficacy due to lack of proper absorption. In the same survey, these physicians generally agreed that an upper nasal delivery would have the potential to provide fast and consistent relief.

DHE is an acute therapy and an alternative to existing treatments that has been used for more than 60 years to safely and effectively treat migraine. DHE is widely used as part of a standard of care for treatment of migraines, despite being limited to IV and injection delivery or traditional nasal administration. IV and injection delivery require administration in physicians' offices, migraine clinics and hospitals, and traditional nasal administration has been challenged by inconsistent efficacy. The AUC of DHE in the first two hours of exposure, or $AUC_{0\text{-}2hr}$, is thought to be critical for achievement of pain relief in acute migraine. Many headache specialists consider DHE to be the current standard of care for the treatment of status migrainosus, which is a condition characterized by debilitating migraines that last more than 72 hours. Unlike triptans, DHE is known to bind to multiple receptors theorized to be implicated in migraine onset and duration. DHE also offers fast-onset efficacy, with continued protection from a single dose at any point during an attack. DHE overcomes many of the limitations of other existing treatments but in its current methods of administration present a number of limitations resulting in unmet needs for migraine patients, including:

- *Need for More Convenient and Consistent Dosing.* DHE is available for administration both intravenously and nasally. Intravenous administration of DHE requires the supervision of a healthcare provider and is typically performed in a headache clinic or hospital setting, requiring the patient to travel while suffering with the migraine.

DHE administrated nasally with traditional, lower space devices may lead to inconsistent dosing and slower speed of effect and pain relief.

- *Opportunity for an Improved Tolerability Profile Compared to Intravenous Administration.* One of the common side effects of conventional DHE administered intravenously is nausea, which is thought to be due to the high C_{max}. Patients who receive DHE intravenously are usually administered an anti-nausea medication beforehand.

A survey of neurologists commissioned by us found that most neurologists are familiar with DHE and its mechanism of action as an acute therapy for migraine, and nearly all are interested in a new DHE delivery system.

Our Solution: Trudhesa

We believe Trudhesa has the potential to be a preferred therapy for the acute treatment of migraines. Trudhesa delivers DHE to the richly-vascularized upper nasal space, offering the potential for rapid and consistent biodistribution without injection. We believe that Trudhesa provides patients with the following benefits when compared to existing migraine therapeutics:

- *Rapid Onset*. The delivery of DHE through our POD technology may offer rapid onset of pain relief similar to IV DHE and investigational pulmonary inhaled DHE (MAP0004). As observed in our completed studies, Trudhesa administration resulted in a total plasma exposure of DHE in the first two hours of dosing (at 1595 pg*h/mL) similar to that seen after MAP0004 dosing (1447 pg*h/mL).
- *Long-lasting*. DHE has been shown to interact with multiple receptors theorized to be implicated in migraine onset and duration. The durability of effect, as observed in our exploratory efficacy analyses by lower migraine recurrence with Trudhesa (7% at 24 hours and 14% at 48 hours for all migraine attacks, weeks 1 - 24) versus triptans (45%), is likely attributable to longer-lasting effect at receptors such as 5-HT1B and 5HT-1D. In our Phase 1 clinical trial, Trudhesa was observed to have similar blood levels of DHE compared to IV DHE from measurements at 30-minutes through 48-hour.
- *Broad Target Population*. Based on historical DHE use, Trudhesa, like other forms of DHE, may provide a higher response rate than triptans and has the potential to treat patients who have not previously responded to triptans or gepants. Similar to other forms of DHE, Trudhesa may also be effective against patients who suffer from morning migraine, severe and prolonged migraine, or menstrual migraine. Migraine treatment with DHE has also demonstrated efficacy, independent of when the migraine treatment is initiated, based on DHE reversing central sensitization, while triptans are ineffective once the migraine becomes centralized.
- *Convenient and Consistent Delivery.* Trudhesa is non-injectable, with the DHE dose delivered in 3/10ths of a second with minimal coordination from the patient. Trudhesa has demonstrated more consistent blood levels than traditional nasal spray, yielding improved blood levels and a lower coefficient of variance with doses. Further, in our STOP 301 trial, 84% of trial participants agreed or strongly agreed with the statement that Trudhesa was “easy to use” and preferred it over their current therapy.
- *Low Incidence of Side Effects.* Nausea and vomiting related to DHE therapy are linked to the high C_{max} related to IV administration. In our completed clinical trials, Trudhesa has shown to be generally well-tolerated with few instances of nausea and vomiting. In fact, it was self-reported in less than 1% of the 6,332 doses of Trudhesa administered over the full duration of the STOP 301 trial.
- *Reducing the Need for Additional Healthcare Resources for Acute Treatment of Migraines*. Exposure Adjusted Event Rate, or EAER, data from our STOP 301 trial showed a significant reduction in the usage of healthcare resources by patients treated with Trudhesa versus their baseline. By reducing the need for emergency room visits for patients with migraines, Trudhesa has the potential to improve patients’ quality of life and reduce resource strain on healthcare facilities.

STOP 301 Trial Results

Our STOP 301 trial conducted in the United States evaluated the safety and tolerability of long-term, intermittent use of Trudhesa in 354 patients for 24 weeks, with 74% of patients completing the treatment period, with a subset of 73 patients continuing for up to a total of 52 weeks, with 90% of continuing patients completing this extended treatment period. In total, 5,273 migraines were treated over the first 48 weeks and approximately 5,650 migraines were treated over the full trial, with 6,332 doses of Trudhesa administered in total. We completed the trial and announced positive top-line data in June 2020, and we submitted data from this trial, along with the Phase 1 pharmacokinetic trial (STOP 101), in our NDA submission in November 2020. Both STOP 101 and STOP 301 results have been peer reviewed and published in the journal Headache.

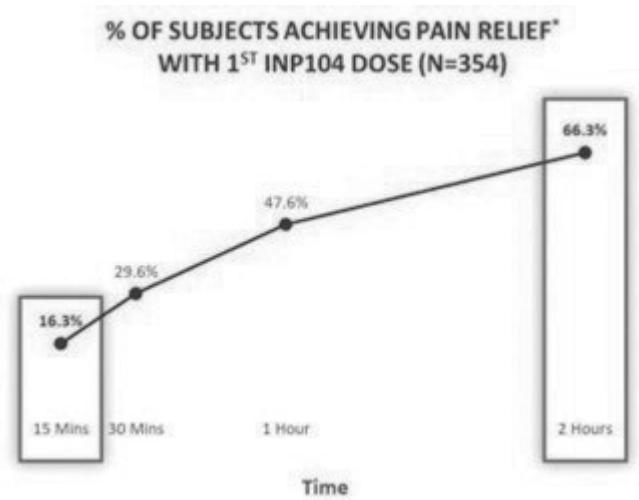
The STOP 301 trial consisted of a four-week screening period, a 24-week treatment period for all participants, a 28-week treatment period extension with a sufficient number of participants to ensure 150 and 50 evaluable data sets in the 24 and 52 week periods, respectively, and a two-week post-treatment follow-up period for all participants. This was an outpatient trial in patients who currently suffer a minimum of two migraines per month. During the trial, participants were instructed on how to self-administer Trudhesa. The primary endpoints of the clinical trial were:

- treatment emergent adverse events, or TEAEs;
- change in nasal mucosa as measured by focused, endoscopic nasal exams conducted by an ear, nose and throat physician following the Nasal Examination Manual; and
- change in olfactory function as assessed by the University of Pennsylvania Smell Identification Test.

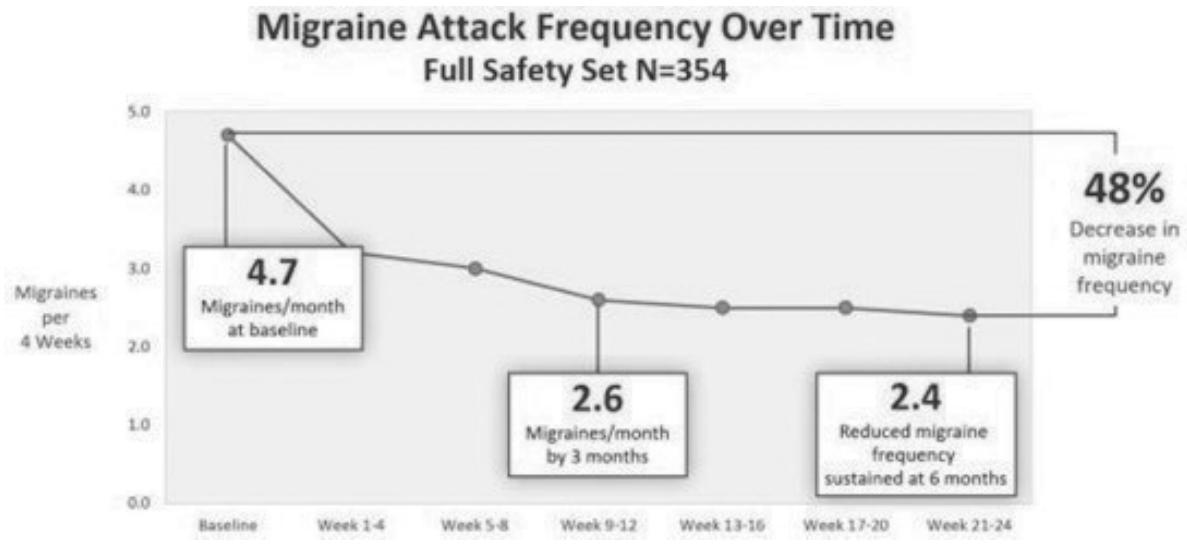
In the trial, Trudhesa was generally well-tolerated. There were seven SAEs among five patients (1.4%) over the 52-week study. Three patients had one SAE each, consisting of one event each of ovarian mass, intestinal obstruction and miscarriage. Two patients had more than one SAE: one patient with pulmonary embolism and visual impairment and one patient with clavicle and rib fractures. None of the SAEs were nasal-related and none of the SAEs were determined by the trial investigator to be related to Trudhesa or led to withdrawal from the trial. There were also no clinically significant changes in olfactory function, and no abnormal findings from endoscopy examinations. There were no serious Trudhesa-related TEAEs, and the majority of Trudhesa-related TEAEs were mild and transient, with the most frequent during the entire 52-week study period being nasal congestion (reported by 17.8% of patients), nausea (6.8%), nasal discomfort (6.8%), abnormal olfactory test (6.8%) and vomiting (2.7%). There were no cardiac adverse events and the discontinuation rate due to adverse events was only 6.8%. While the 28 -week trial extension was initiated to gather additional data on long term use of Trudhesa up to 52 weeks, ultimately the extension was unnecessary per trial protocol due to lack of safety signals in the 24-week cohort.

Exploratory efficacy measures were captured consisting of reporting in an electronic diary the time of onset of a migraine and associated symptoms, such as nausea, vomiting, sound sensitivity, smell sensitivity and light sensitivity. After taking a dose of Trudhesa, questions about the severity of, and relief from, all symptoms were repeated at 15 minutes, 30 minutes and 1, 2, 8, 24 and 48 hours post dosing. Patients were also required to undergo periodic evaluation using Migraine Disability Assessment, or MIDAS, and Headache Impact Test, or HIT-6, questionnaires.

The trial evaluated the acute treatment effects of Trudhesa against the patient's best previous migraine treatment and the long-term effects of Trudhesa utilized by patients for 24 weeks as exploratory efficacy endpoints. While not conducted with a parallel control group and not powered for statistical significance, on their first dose of Trudhesa, 38% of patients reported being pain free at two hours. This effect remained consistent with long-term administration as 39% of all patients treated with Trudhesa through 12 weeks had pain freedom at two hours (2,559 total migraines), and 35% of all patients treated with Trudhesa through 24 weeks had pain freedom at two hours (1,736 total migraines). Trudhesa was also associated with a reduction in pain symptoms, as 52% of patients receiving Trudhesa were free of their most bothersome migraine symptom at two hours. Further, as shown in the figure below, 16% of patients who were treated with Trudhesa had pain relief within 15 minutes and 66% of patients had pain relief within 2 hours (N=354).



The long-term nature of the STOP301 trial also provided notable long-term data on the continued administration of Trudhesa in an exploratory efficacy analysis conducted as part of the trial. As reflected in the figure below, patients treated with Trudhesa reported a 48% reduction in the frequency of their migraines over baseline during the 24-week trial.



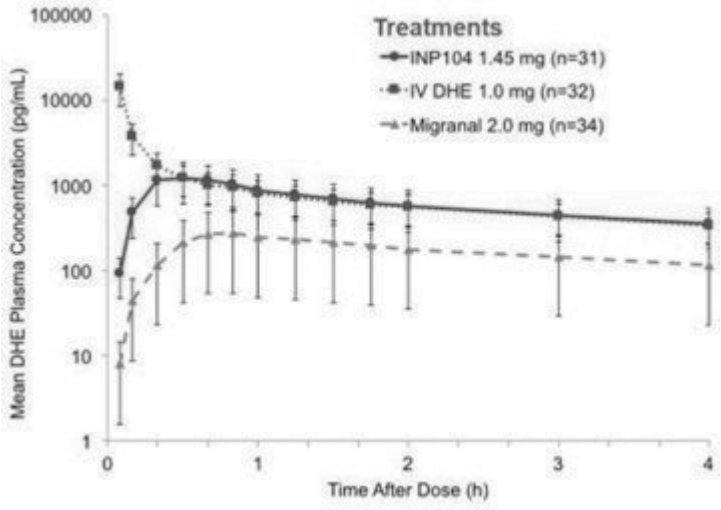
Pain freedom was consistent across multiple attacks throughout the 52-week treatment period, with between 31%-39% of patients in each measurement period achieving pain freedom at two hours. Additionally, 93% and 86% of patients achieving pain freedom at two hours on Trudhesa did not suffer a relapse in migraine or require a rescue medication at 24 hours and 48 hours, respectively throughout the 24 weeks.

EAER data also showed a meaningful reduction in the usage of healthcare resources by patients treated with Trudhesa versus their baseline. Specifically, emergency room visits were reduced by approximately 73% and hospitalizations and urgent care visits were reduced by 100%.

Phase 1 Clinical Trial Results

We completed a randomized three-way crossover pivotal Phase 1 clinical trial in the fourth quarter of 2017. Thirty-six healthy volunteers in Australia were randomized, and 27 were included in the evaluation of pharmacokinetic measures and comparative bioavailability. Migranal and Trudhesa were self-administered by the trial participants. Migranal is an FDA-approved nasal spray product using the same liquid formulation of DHE, but delivered with a traditional nasal spray to the lower nasal space. The primary endpoint was to compare the bioavailability of DHE following single dose administration of 1.45 mg Trudhesa, 1mg IV DHE as a “safety bridge” and 2mg Migranal as an “efficacy bridge”. Pharmacokinetic measures, which refers to the movement of drug through the body, were recorded from baseline through 48 hours, with measures taken at 5, 10, 20, 30, 40 50 and 60 minutes within the first hour, and then at 3, 4, 8, 12, 24, 36 and 48 hours. Secondary endpoints were to evaluate the safety and tolerability of single doses of Trudhesa and to assess plasma concentrations of 8’-hydroxy-dihydroergotamine, the primary metabolite of DHE.

Despite containing approximately 28% less DHE per dose than Migranal, Trudhesa achieved blood levels comparable to IV DHE from 30 minutes, which quickly separated from Migranal blood levels at five minutes, achieved T_{max} more rapidly, achieved a four-fold increase in C_{max} and a three-fold increase in AUC. After 20 minutes, Trudhesa reached 93% of its C_{max} and sustained DHE levels similar to those seen with IV dosing from 30 minutes through to 48 hours. The following figure shows the pharmacokinetic measurements of DHE with Trudhesa, IV DHE and Migranal for the first four hours after dosing.



Unlike standard bioequivalence studies, the intent of this trial was to investigate whether C_{max}, AUC and T_{max} of Trudhesa lay between the 90% confidence intervals of IV DHE and Migranal. This would permit a "scientific bridge" to the FDA's findings of safety data for the IV product, with higher blood levels, and to the FDA's efficacy findings for Migranal, with lower blood levels. As the following table indicates, Trudhesa met the preplanned statistical endpoints to satisfy this recommendation from the FDA with statistical power in excess of 95% on all endpoints. Our proprietary POD technology demonstrated more consistent dosing than a traditional nasal spray as seen with the lower coefficient of variance measures of plasma levels compared to Migranal as highlighted in the table below.

DHE Pharmacokinetics (STOP 101 – PK population (n=27))

	Migranal (2mg)		Trudhesa (1.45mg)		D.H.E.45 IV (1mg)	
$AUC_{0\text{-}inf}$ (pg*hr/ml) [%CV]	2,208	[67%]	6,153	[44%]	7,490	[15%]
C_{max} (pg/ml) [%CV]	329	[79%]	1,281	[53%]	14,620	[34%]
T_{max}, median (min)	4740		30		5	
$AUC_{0\text{-}2}$ (hr*pg/ml)	429		1,595		3,019	

Trudhesa was generally well-tolerated, with no participants experiencing serious adverse events that were drug related. The most common treatment-related adverse events observed for Trudhesa included drowsiness, headaches and muscle soreness. Participants of this trial were surveyed on preference in administration, and Trudhesa was preferred three to one over Migranal. Trudhesa was noted to have less dripping, less post-nasal drip, was viewed as easier to use and over two-thirds of the volunteers were "quite satisfied" or "very satisfied" with nasal delivery experience with our proprietary POD technology.

Optimized DHE delivery has been shown to yield rapid and sustained clinical benefit in pain relief and pain freedom in the acute treatment of migraines. $AUC_{0\text{-}2hr}$ is thought to be critical for achievement of pain relief. In a pharmacokinetic clinical trial of MAP0004, an investigational pulmonary inhaled DHE product that has not been approved by the FDA, an $AUC_{0\text{-}2hr}$ of 1,447 pg*hr/mL was observed.

Commercialization Strategy for Trudhesa

Given the concentrated prescriber base of our target market for Trudhesa, we independently launched in October 2021. Trudhesa was launched with an initial sales force of 60 representatives and was recently expanded to approximately 90 representatives to support our targeted launch strategy. The current listed WAC price of Trudhesa is $892.50 for four doses (1 pack). Through December 31, 2022, there have been approximately 58,420 prescriptions of Trudhesa generated since launch and, based on third-party data, we believe Trudhesa accounts for approximately 4.3% of total branded acute migraine prescriptions among over 2,000 unique Trudhesa prescribers since launch. Additionally, based on internal data, approximately 63% of new Trudhesa patients eligible for a refill have received a second prescription. The sales team is supported by an established market access, medical affairs, marketing, and operations infrastructure. Our commercial efforts are focused on approximately 11,000 high value HCP targets that prescribe approximately 40% of all migraine total prescriptions and 73% of all acute branded total prescriptions. Importantly, we have secured managed care contracts providing access to Trudhesa for approximately 80% of commercial lives in the United States. We have deployed a robust sample program to ensure trial with Trudhesa for patients seeking better treatments and outcomes. Through both our

commercial and medical affairs infrastructure we have engaged healthcare practitioners and patients, partnered with national associations and actively supported advocacy groups in the migraine market. These efforts have been, and will continue to be, supplemented with non-personal promotion to all targeted and non-targeted medium value physicians. To capture the maximum commercial opportunity of Trudhesa, we may also selectively seek partners to commercialize the product outside of our target markets, including additional penetration within the broader primary care setting, as well as in geographies outside of the United States.

Manufacturing

All of our manufacturing processes are outsourced to third parties with oversight by our internal managers. We rely on third-party manufacturers to comply with current good manufacturing practices, or cGMP, and produce sufficient quantities of drug product for use in clinical trials and Trudhesa sales.

The active pharmaceutical ingredient and drug formulation of Trudhesa has been developed and manufactured by a contract manufacturing organization, or CMO, located in Europe. Our CMO has extensive experience manufacturing the liquid formulation of dihydroergotamine mesylate under cGMP and has the capacity to manufacture at commercial scale. This CMO has manufactured Migranal, a drug that uses the same primary container and formulation as Trudhesa, for over 20 years. The DHE batches used in the pivotal Phase 1 clinical trial, our registration lots, and our STOP 301 trial were all produced by the same manufacturer, and on the same manufacturing lines that have been used for commercial launch of Trudhesa.

The Trudhesa POD device is manufactured by third-party CMOs. This device has been used for the pivotal Phase 1 clinical trial, our registration lots, and our STOP 301 trial and is the device used for commercial launch of Trudhesa. The plastic component manufacturing and sub-assembly, valve manufacture, canister manufacture and canister fill with final assembly are each performed by a different third-party CMO. Each have extensive experience with medical-grade clinical and commercial scale device manufacture under cGMP. We used the same assembly group through all stages of development and have utilized the same assembly lines and validated processes through the NDA approval and submission process and for commercial production.

Competition

The pharmaceutical industry is highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations actively engaged in research and development of product candidates which may target the same markets as our historical product candidates. We expect any future product candidates we develop to compete on the basis of, among other things, product efficacy and safety, time to market, price, extent of adverse side effects experienced and convenience of administration and drug delivery.

For Trudhesa, we are aware of several competing efforts. Approved acute treatments for migraine include triptans, ditans, oral calcitonin gene-related peptides antagonists or gepants (such as Zavzpret™ and Nurtec® both commercialized by Pfizer Inc.), lasmiditan and alternative formulations of DHE, such as Migranal, which is administered intranasally. Some of these competitors are also developing product candidates that utilize alternative routes of administration, Amneal Pharmaceuticals, Inc., Satsuma Pharmaceuticals, Inc. and Zosano Pharma Corporation, whose product candidates use nasal pumps, other nasal drug delivery or alternative delivery technologies.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Accelerated merger and acquisition activity in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited in the event that our competitors develop and commercialize product candidates that are more effective, safer, less toxic, more convenient or less expensive than our comparable product candidates. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our product candidates. We believe the factors determining the success of our programs will be the efficacy, safety and convenience of our product candidates.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and product candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover, but is not limited to, our POD technology, our historical product candidates and components thereof, their methods of use and processes for their manufacture, and any other inventions that are commercially important to our business. We expect to rely on data exclusivity, market exclusivity, patent term adjustment and patent term extensions when available. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patents; to defend against and challenge the assertion by third parties of their purported intellectual property rights; and to operate without the unauthorized infringement on the valid and enforceable patents and other proprietary rights of third parties.

We believe that we have a strong global intellectual property position relating to our POD device, Trudhesa and our prior product candidates. Our patent portfolio as of February 1, 2023 contained 14 U.S. issued patents and 74 patents issued in ex-U.S. jurisdictions including Australia, Belgium, Brazil, Canada, China, Switzerland, Germany, France, Great Britain, India, Israel, Italy, Japan, Mexico, Luxembourg, Netherlands, New Zealand, Spain, and South Africa, and 13 U.S. pending applications as well as 67 patent applications pending in ex-U.S. jurisdictions including Australia, Brazil, Canada, Chile, China, Europe, Hong Kong, Israel, India, Japan, Korea, Mexico, New Zealand, and Singapore, owned solely by us.

Trudhesa is covered by five patent families: three of the families include claims relating to the POD device used for delivery of DHE to the upper nasal cavity; the other two families include claims relating to methods of delivering DHE to the upper nasal cavity. As of February 1, 2023, from the three device patent families, six U.S. patents have issued, 45 patents have issued in ex-U.S. jurisdictions including Australia, Brazil, Canada, China, Switzerland, Germany, France, Great Britain, Israel, India, Japan, Mexico, New Zealand, Russia, and South Africa, and 10 applications were pending in the U.S., Canada, Europe, India, and Korea. Six issued U.S. patents are listed on the FDA Orange Book. As of February 1, 2023, from the two method of use patent families, one U.S. Patent has issued, and 11 patents have issued in ex-U.S. jurisdictions including Australia, Belgium, Canada, Switzerland, Germany, Spain, France, Great Britain, Italy, Luxembourg, and the Netherlands, two applications were pending in the U.S., and 15 applications were pending in ex-U.S. jurisdictions including Australia, Brazil, Canada, China, Europe, India, Japan, Hong Kong, and Korea. Our issued patents, and any patents that may issue from our pending patent applications, are expected to expire between 2032 and 2039, absent any patent term adjustments.

In addition, we have exclusively licensed a patent portfolio that as of February 1, 2023, contained two U.S. issued patents and nine patents issued in ex-U.S. jurisdictions including Canada, Italy, Great Britain, France, Spain, and Germany. This patent portfolio includes claims relating to a circumferential aerosol device for delivering drugs including to the olfactory epithelium and brain. Our issued patents that have been licensed are expected to expire between 2029 and 2031, absent any patent term adjustments or extensions. None of our licensed patents are material to our prior product candidates.

We continually assess and refine our intellectual property strategy as we develop new platform technologies and product candidates. To that end, we are prepared to file additional patent applications if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. Further, we are prepared to file patent applications, as we consider appropriate under the circumstances, relating to the new technologies that we develop. In addition to filing and prosecuting patent applications in the United States, we often file counterpart patent applications in Europe and in additional countries where we believe such foreign filing is likely to be beneficial.

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. However, the term of U.S. patents may be extended for delays incurred encountered during prosecution that are caused by the USPTO or due to compliance with FDA requirements. For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond five years, nor beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions of our issued patents in any jurisdiction where these are available; however, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such extensions

should be granted, and even if granted, the length of such extensions. Our currently issued patents, including those owned and exclusively licensed, will likely expire on dates ranging from 2029 to 2039. If patents are issued on our pending patent applications, including those owned and exclusively licensed, the resulting patents are projected to expire on dates ranging from 2032 to 2040, unless we receive patent term adjustment or patent term extension, or both. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of CNS diseases has emerged in the United States. The patent situation outside of the United States is even more uncertain. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending, and enforcing patent claims that cover our technology, inventions, and improvements. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our platforms and product candidates and the methods used to manufacture those platforms and product candidates.

Our issued patents and those that may issue in the future may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related platforms or product candidates or limit the length of the term of patent protection that we may have for our POD device and product candidates. In addition, 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. For these reasons, we may have competition for our POD device and 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 related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent. For this and more comprehensive risks related to our proprietary technology, inventions, improvements, platforms and product candidates, please see the section titled “Risk Factors—Risks Related to Intellectual Property.”

Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our platform’s product candidates. Third parties may have, or may obtain, blocking patents that could be used to prevent us from commercializing our POD device and product candidates and practicing our proprietary technology.

We own trademark registrations and pending applications for use in connection with Trudhesa and our prior product candidates in several jurisdictions, including the United States. The IMPEL mark is registered in Austria, Canada, China, the European Union, India, Japan, Mexico, South Korea, United Kingdom, and the United States. The IMPEL mark in simplified Chinese characters mark is registered in China. The IMPEL mark with the Impel Logo is registered in Australia. The Impel Logo is registered in Australia, Canada, China, the European Union, India, Japan, Mexico, South Korea, United Kingdom, and the United States. We own pending applications for the Impel Dots Logo in Australia, Canada, China, the European Union, Japan, Mexico, South Korea, the United Kingdom, and the United States. The POD mark is registered in Australia, the European Union, India, United Kingdom, and the United States. The IMPELPOD mark is registered in China, Japan, and South Korea, and we own a pending application in Canada. The TRUDHESA mark is registered in Australia, China, the European Union, India, Japan, Mexico South Korea, the United Kingdom, and the United States and we own a pending application in Canada. The Trudhesa logo is registered in the United States.

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. These agreements provide that all confidential information concerning our business or financial affairs 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. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our confidentiality and other agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors require them to assign or grant us licenses to inventions they

invent as a result of the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions.

We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting inventions.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products and medical devices. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as a clinical hold, FDA refusal to approve a pending NDA, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product CMC, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue 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 trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practices, or GCPs, which are standards meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an investigational review board, or IRB, for approval. An IRB may also require the clinical

trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial may be sufficient in rare instances, including (1) where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, currently exceeding $3,200,000 for Fiscal Year 2023. The manufacturer or sponsor under an approved NDA is also subject to an annual program fee, currently exceeding $390,000 for each prescription drug product for Fiscal Year 2023. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for standard review drug products that are not new molecular entities, or NMEs, are reviewed within ten months of the date of submission of the NDA to the FDA; most applications for priority review drugs that are not NMEs are reviewed within six months of the date of submission of the NDA to the FDA. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will generally inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with cGMP is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to,

special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained, or problems are identified following initial marketing. No REMS was required for Trudhesa.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Section 505(b)(2) New Drug Applications

An alternative to the 505(b)(1) NDA pathway described above is an NDA submitted under Section 505(b)(2) of the FDCA, which enables the applicant to rely, in part, on the FDA's prior findings in approving a similar product or published literature in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for modified formulations, new routes of administration, or new uses of previously approved products.

Section 505(b)(2) permits the submission of an NDA where at least some of the safety and efficacy information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's prior findings of safety or effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant. The Trudhesa NDA was filed under Section 505(b)(2) and referred to both the approved IV DHE product (D.H.E. 45) and Migranal.

Fast Track Designation

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment, and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for Fast Track Designation within 60 days of receipt of the sponsor's request.

Under the Fast Track program, the FDA may grant Fast Track Designation for a drug if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. 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.

If a submission is granted Fast Track Designation, the sponsor may engage in more frequent interactions with the FDA, and the FDA may initiate review of sections of the NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, Fast Track Designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information on ClinicalTrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can

be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers or deferrals for submission of data.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMP after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMP. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The FDA strictly regulates marketing, labeling, advertising and promotion of drugs that are placed on the market. Advertising and promotion of drugs must be in compliance with the FDCA and its implementing regulations and only for the approved indications and in a manner consistent with the approved labeling. 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, including investigation by federal and state authorities.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii)

the listed patent has expired; the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

To the extent that a Section 505(b)(2) applicant is relying on the FDA's prior findings of safety or effectiveness for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Thus, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Exclusivity

Upon NDA approval of a new chemical entity, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period of exclusivity if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application. FDA cannot approve an ANDA for a generic drug that includes the change during the exclusivity period.

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, for example new indications, dosages or strengths of an existing drug. 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.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval up to a maximum of five years). The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years, and only one patent can be extended. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Combination Products

A combination product is a product comprising (i) two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprising drug and device products, device and biological products, or biological and drug products; (iii) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, for example, to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (iv) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various branches, or Centers, by product type. Different Centers typically review drug, biologic, or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product becomes the lead evaluator. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, an applicant submits a single marketing application to the Center selected to be the lead evaluator, although separate applications for each constituent part may be submitted to the applicable Centers. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

In a drug/device combination product, where the device component is a prefilled drug delivery device, the primary mode of action is typically a drug mode of action with the Center for Drug Evaluation and Research, or CDER, as the lead Center. CDER would review the NDA in consultation with the Center for Devices and Radiological Health (CDRH) on device-specific issues. For co-packaged or single-entity combination products, such as pre-filled drug-delivery devices, there are two ways to comply with cGMP requirements. Manufacturers can either (i) demonstrate compliance with all cGMP regulations applicable to each of the constituent parts in the combination product or (ii) in the case of drug-device combination products, demonstrate compliance with either the drug cGMP regulations or the device Quality System Regulation, or QSR, and also demonstrate compliance with additional provisions from the other of these two sets of cGMP requirements, as specified in the combination products regulations.

Failure to comply with applicable regulatory requirements can result in enforcement action by the FDA, which may include any of the following sanctions: warning or untitled letters, fines, injunctions, civil or criminal penalties, recall or seizure of current or future products, operating restrictions, partial suspension or total shutdown of production, refusal or denial of submissions for new products, or withdrawal of clearance, authorization, or approval.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain general business and marketing practices in the pharmaceutical industry. These laws include anti-kickback statutes, false claims, transparency, and health information privacy laws and other healthcare laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Affordable Care Act, or ACA, amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to commit a violation. 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. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicare and Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the ACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability under the federal False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and civil False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the additional federal criminal statutes created by the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published on January 25, 2013, impose obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their business associates that perform certain services involving the storage, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, and often are not preempted by HIPAA.

Further, pursuant to the ACA, the CMS has issued a final rule that requires manufacturers of prescription drugs to collect and annually report information on certain payments or transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, certified nurse-midwives, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. The reported data is made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, certain states require pharmaceutical companies to implement compliance programs or marketing codes. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Efforts to ensure that business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. If a drug company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment, and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a drug company

to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Reimbursement

The regulations that govern pricing and reimbursement for new drugs and therapeutic biologics vary widely from country to country. Some countries require approval of the sale price of a drug or therapeutic biologic before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, a drug company can obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of that product.

A drug company's ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government authorities, private health insurers and other organizations. Even if one or more products are successfully brought to the market, these products may not be considered cost-effective, and the amount reimbursed for such products may be insufficient to allow them to be sold on a competitive basis. Increasingly, third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for pharmaceutical products.

Significant delays can occur in obtaining reimbursement for newly-approved drugs or therapeutic biologics, and coverage may be more limited than the purposes for which the drug or therapeutic biologic is approved by the FDA or similar foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug or therapeutic biologic will be reimbursed in all cases or at a rate that covers a drug company's costs, including research, development, manufacture, sale and distribution.

Interim reimbursement levels for new drugs or therapeutic biologics, if applicable, may also be insufficient to cover a drug company's costs and may not be made permanent. Reimbursement rates may be based on payments allowed for lower cost drugs or therapeutic biologics that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs or therapeutic biologics 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 or therapeutic biologics from countries where they may be sold at lower prices than in the United States. Further, no uniform policy for coverage and reimbursement exists in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement can differ significantly from payor to payor.

Government Pricing and Reimbursement Programs for Marketed Drugs in the United States

Medicaid, the 340B Drug Pricing Program, and Medicare

Federal law requires that a pharmaceutical manufacturer, as a condition of having its products receive federal reimbursement under Medicaid and Medicare Part B, must pay rebates to state Medicaid programs for all units of its covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program under either a fee-for-service arrangement or through a managed care organization. This federal requirement is effectuated through a Medicaid drug rebate agreement between the manufacturer and the Secretary of U.S. Department of Health and Human Services, or HHS. The Centers for Medicare & Medicaid Services, or CMS, administers the Medicaid drug rebate agreements, which provide, among other things, that the drug manufacturer will pay rebates to each state Medicaid agency on a quarterly basis and report certain price information on a monthly and quarterly basis. The rebates are based on prices reported to CMS by manufacturers for their covered outpatient drugs. For non-innovator products, generally generic drugs marketed under abbreviated new drug applications, the rebate amount is 13% of the average manufacturer price, or AMP, for the quarter. The AMP is the weighted average of prices paid to the manufacturer (1) directly by retail community pharmacies and (2) by wholesalers for drugs distributed to retail community pharmacies. For innovator products (i.e., drugs that are marketed under NDAs or BLAs), the rebate amount is the greater of 23.1% of the AMP for the quarter or the difference between such AMP and the best price for that same quarter. The best price is essentially the lowest price available to non-governmental entities. Innovator products may also be subject to an additional rebate that is based on the amount, if any, by which the product's AMP for a given quarter exceeds the inflation-adjusted baseline AMP, which for most drugs is the AMP for the first full quarter after launch. Since 2017, non-innovator products are also subject to an additional rebate. To date, the rebate amount for a drug has been capped at 100% of the AMP; however, effective January 1, 2024, this cap will be eliminated,

which means that a manufacturer could pay a rebate amount on a unit of the drug that is greater than the average price the manufacturer receives for the drug.

The terms of participation in the Medicaid drug rebate program impose an obligation to correct the prices reported in previous quarters, as may be necessary. Any such corrections could result in additional or lesser rebate liability, depending on the direction of the correction. In addition to retroactive rebates, if a manufacturer were found to have knowingly submitted false information to the government, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

A manufacturer must also participate in a federal program known as the 340B drug pricing program in order for federal funds to be available to pay for the manufacturer's drugs under Medicaid and Medicare Part B. Under this program, the participating manufacturer agrees to charge certain safety net healthcare providers no more than an established discounted price for its covered outpatient drugs. The formula for determining the discounted price is defined by statute and is based on the AMP and the unit rebate amount as calculated under the Medicaid drug rebate program, discussed above. Manufacturers are required to report pricing information to the Health Resources and Services Administration, or HRSA, on a quarterly basis. HRSA has also issued regulations relating to the calculation of the ceiling price as well as imposition of civil monetary penalties for each instance of knowingly and intentionally overcharging a 340B covered entity.

Federal law also requires that manufacturers report data on a quarterly basis to CMS regarding the pricing of drugs that are separately reimbursable under Medicare Part B. These are generally drugs, such as injectable products, that are administered incident to a physician service and are not generally self-administered. The pricing information submitted by manufacturers is the basis for reimbursement to physicians and suppliers for drugs covered under Medicare Part B. As with the Medicaid drug rebate program, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

Medicare Part D provides prescription drug benefits for seniors and people with disabilities. Medicare Part D enrollees once had a gap in their coverage (between the initial coverage limit and the point at which catastrophic coverage begins) where Medicare did not cover their prescription drug costs, known as the coverage gap. However, beginning in 2019, Medicare Part D enrollees paid 25% of brand drug costs after they reached the initial coverage limit - the same percentage they were responsible for before they reached that limit - thereby closing the coverage gap from the enrollee's point of view. Most of the cost of closing the coverage gap is being borne by innovator companies and the government through subsidies. Each manufacturer of drugs approved under NDAs or BLAs is required to enter into a Medicare Part D coverage gap discount agreement and provide a 70% discount on those drugs dispensed to Medicare Part D enrollees in the coverage gap, in order for its drugs to be reimbursed by Medicare Part D. Beginning in 2025, the IRA eliminates the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. Although these discounts represent a lower percentage of enrollees' costs than the current discounts required below the out-of-pocket maximum (that is, in the coverage gap phase of Part D coverage), the new manufacturer contribution required above the out-of-pocket maximum could be considerable for very high-cost patients and the total contributions by manufacturers to a Part D enrollee's drug expenses may exceed those currently provided.

The IRA will also allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in October 2022 for Medicare Part D and January 2023 for Medicare Part B, the IRA will also penalize drug manufacturers that increase prices of Medicare Part D and Part B drugs at a rate greater than the rate of inflation.

U.S. Federal Contracting and Pricing Requirements

Manufacturers are also required to make their covered drugs, which are generally drugs approved under NDAs or BLAs, available to authorized users of the Federal Supply Schedule (FSS) of the General Services Administration. The law also requires manufacturers to offer deeply discounted FSS contract pricing for purchases of their covered drugs by the Department of Veterans Affairs, the Department of Defense, the Coast Guard, and the Public Health Service (including the Indian Health Service) in order for federal funding to be available for reimbursement or purchase of the manufacturer's drugs under certain federal programs. FSS pricing to those four federal agencies for covered drugs must be no more than the Federal Ceiling Price, or FCP, which is at least 24% below the Non-Federal Average Manufacturer Price, or Non-FAMP, for the prior year. The Non-FAMP is the average price for covered drugs sold to wholesalers or other middlemen, net of any price reductions.

The accuracy of a manufacturer's reported Non-FAMPs, FCPs, or FSS contract prices may be audited by the government. Among the remedies available to the government for inaccuracies is recoupment of any overcharges to the four specified federal agencies based on those inaccuracies. If a manufacturer were found to have knowingly reported false prices, in addition to other penalties available to the government, the law provides for significant civil monetary penalties per incorrect item. Finally, manufacturers are required to disclose in FSS contract proposals all commercial pricing that is equal to or less than the proposed FSS pricing, and subsequent to award of an FSS contract, manufacturers are required to monitor certain commercial price reductions and extend commensurate price reductions to the government, under the terms of the FSS contract Price Reductions Clause. Among the remedies available to the government for any failure to properly disclose commercial pricing and/or to extend FSS contract price reductions is recoupment of any FSS overcharges that may result from such omissions.

U.S. Healthcare Reform

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. On September 9, 2021, the Biden administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. These proposals recently culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which will, among other things, allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in January 2023 for Medicare Part B and October 2022 for Medicare Part D, the IRA will also penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges.

Further, additional state and federal healthcare reform measures may be adopted in the future.

Employees and Human Capital Resources

Employees

As of December 31, 2022, we had 160 full-time employees and four full-time contract employees. Of these employees, 14 have an M.D. or a Ph.D. From time to time, we also retain consultants to support our organization. As of December 31, 2022, we had 12 consultants. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

Diversity and Inclusion

We are committed to creating and maintaining a workplace free from discrimination or harassment on the basis of color, race, sex, national origin, ethnicity, religion, age, disability, sexual orientation, gender identification or expression or any other status protected by applicable law. Our management team and employees are expected to exhibit and promote honest, ethical and respectful conduct in the workplace.

Competitive Pay & Benefits

We strive to provide pay, comprehensive benefits and services that help meet the varying needs of our employees. Our total rewards package includes competitive pay; comprehensive healthcare benefits package for employees. In addition, we offer every full-time employee, both exempt and non-exempt, the benefit of equity ownership in the company through stock option grants.

Employee Development & Training

We focus on attracting, retaining, and cultivating talented individuals. We emphasize employee development and training by providing access to a wide range of online and instructor led development and continual learning programs.

Employees are encouraged to attend scientific, clinical and technological meetings and conferences and have access to broad resources they need to be successful.

Corporate Information

We were incorporated under the laws of the State of Delaware in 2008. In April 2022, we changed our name from Impel NeuroPharma, Inc. to Impel Pharmaceuticals Inc. Our principal executive offices are located at 201 Elliott Avenue West, Suite 260, Seattle, WA 98119, and our telephone number is (206) 568-1466. Our website address is https://impelpharma.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into, this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock.

Available Information

We make available free of charge on our website our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or SEC. The reports are also available at www.sec.gov

Item 1A. Risk Factors.

You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this report.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this report captioned “Risk Factors.” The following is a summary of the principal risks we face:

- We are a commercial-stage biopharmaceutical company and have incurred net losses since our inception. We anticipate that we will continue to incur substantial operating losses for the foreseeable future and we may never achieve or sustain profitability.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates on unfavorable terms to us.
- The development and commercialization of pharmaceutical products is subject to extensive regulation, and we may not obtain regulatory approvals for INP105 or any other additional product candidates.
- Our future commercial success depends upon attaining significant market acceptance of any future product candidates, if approved, among physicians, patients, health care payors and others in the medical community necessary for commercial success.
- Clinical failure may occur at any stage of clinical development, and we may never succeed in developing and commercializing additional marketable product candidates or generating additional product revenue.
- Delays in the commencement, enrollment or completion of clinical trials of any future product candidates, or in the acceptance of foreign clinical trial data, could result in increased costs to us as well as a delay or failure in obtaining regulatory approval, or prevent us from commercializing future product candidates on a timely basis, or at all.
- We rely entirely on third parties for the manufacturing of Trudhesa and any future candidates that we develop for nonclinical studies and clinical trials and expect to continue to do so for commercialization. If we encounter difficulties in negotiating manufacturing and supply agreements with third-party manufacturers and suppliers of

our POD device and the active ingredients in Trudhesa, and any future product candidates, our ability to commercialize such product candidates, if approved, would be impaired.

- If we are not able to obtain and enforce patent protection for our technologies or any future product candidates, development and commercialization of our technology and any future product candidates may be adversely affected.
- We may be required to expand our operations capabilities in the future, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- If we fail to attract and retain senior management and key scientific personnel, we may be unable to successfully develop and commercialize any future product candidates.
- The ongoing COVID-19 pandemic, or similar public health crises, could have a material adverse impact on our business, financial condition and results of operations, including through disruption to our planned clinical trials, supply chains, business operations and commercialization efforts for Trudhesa and any future product candidates.
- The market price of our common stock may be volatile, which could result in substantial losses for investors.

Risks Related to Our Financial Position and Need for Additional Capital

We are a commercial-stage biopharmaceutical company and have incurred net losses since our inception. We anticipate that we will continue to incur substantial operating losses for the foreseeable future and we may never achieve or sustain profitability.

We are a commercial-stage biopharmaceutical company formed in 2008. To date, we have financed our operations primarily through the sale and issuance of redeemable convertible preferred stock, convertible notes and warrants, common stock offerings, debt financings and royalty financings. Since 2021, we have also relied on revenues generated from net sales of Trudhesa.

We have incurred significant net losses since our inception. Our net losses were $106.3 million and $76.7 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $321.1 million. We cannot predict when or whether we will become profitable and we may never be able to develop or commercialize any future product candidates. Our losses have resulted principally from costs incurred in our product candidate discovery and development activities. We expect to incur net losses for the foreseeable future.

Our financial position will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or additional grants. If we are required by the FDA, or any equivalent foreign regulatory authority, to perform clinical trials or studies in addition to those we currently expect to conduct, including if foreign clinical trial data are not accepted by the FDA, or if there are any delays in completing the clinical trials of product candidates, our expenses could increase substantially. Although we have received approval for Trudhesa, the resulting revenue from its commercialization may not enable us to achieve profitability. Even if we obtain regulatory approval to market additional product candidates, our future revenues will depend upon the size of any markets in which such product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for product candidates in those markets.

Our expenses and net losses may increase as we continue to commercialize Trudhesa, continue our development of, and seek regulatory approvals for, other product candidates, and begin to commercialize other approved products as well as hire additional personnel, protect our intellectual property and incur additional costs associated with operating as a public company. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical studies and trials, associated manufacturing needs, commercialization activities if our other product candidates are approved and our expenditures on other research and development activities.

To become and remain profitable, we must expand the market for Trudhesa, successfully develop product candidates, obtain regulatory approval for them, and manufacture, market and sell those product candidates for which we may obtain regulatory approval. We may not succeed in these activities and we may never generate revenue from product sales that are significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business for any reason, including as a result of the COVID-19 pandemic. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on

our stockholders' equity and working capital. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, discover or develop other product candidates or continue our operations.

We will require substantial additional financing to achieve our goals and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of December 31, 2022, we had $60.7 million of cash and cash equivalents. Based upon our current operating plan, we estimate that our cash and cash equivalents as of December 31, 2022, are insufficient for us to fund operating, investing, and financing cash flow needs for twelve months subsequent to the issuance date of the financial statements included in this Annual Report on Form 10-K and accordingly, we have determined that there is substantial doubt about our ability to continue as a going concern. We believe that we will continue to expend substantial resources for the foreseeable future as we continue the commercialization of Trudhesa, develop additional product candidates, if any, and launch clinical trials for such product candidates and pursue commercialization of product candidates, if approved. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of product candidates. Our costs will increase if we suffer any delays in our planned clinical trials for our current product candidates. Our forecast of the period of time through which our financial reserves will adequately support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the cost of commercialization activities for Trudhesa, or any other approved product, including marketing, sales and distribution costs;
- the timing of, and the costs involved in, obtaining regulatory approvals for product candidates if clinical trials are successful;
- the scope, progress, results and costs of developing and advancing product candidates through clinical trials and researching and discovering new product candidates;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the cost of manufacturing product candidates for clinical trials in preparation for regulatory approval and in preparation for commercialization;
- the amount of revenue from Trudhesa and any other approved product candidates, if any; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation.

We will need to raise additional funds to address our goals. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings if available, collaborations, strategic alliances, licensing arrangements, and other marketing or distribution arrangements. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate nonclinical studies, clinical trials or other development activities for one or more product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to continue to commercialize Trudhesa and other future product candidates if approved.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates on unfavorable terms to our business.

We may seek additional capital through a variety of means, including through private and public equity offerings and debt financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of such equity or convertible debt securities may include liquidation or other preferences that are senior to or otherwise adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring

additional debt, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. For example, our loan agreement with Oaktree includes covenants requiring us to provide an audit opinion of our annual financial statements that is not subject to any "going concern" or like qualification or exception and requires us to maintain a minimum $12.5 million unrestricted cash balance at all times. On March 22, 2023, we entered into a letter agreement (the "Oaktree Letter Agreement") in connection with our Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from the going concern explanatory paragraph included the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022. Further, our loan agreement with Oaktree is secured by a lien on substantially all of our assets, and our revenue interest financing agreement Oaktree is secured by accounts receivable arising from net sales of Trudhesa and our intellectual property relating to Trudhesa. If we raise additional funds through strategic partnerships or royalty monetization agreements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not 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 commercialization efforts for any future product candidates, or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

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:

- quarterly fluctuations in product sales of Trudhesa or any other product candidates which may receive regulatory approval;
- variation in the level of expense related to the commercialization of Trudhesa or any other product candidates that receives regulatory approval;
- variations in the level of expense related to the ongoing development of product candidates or future development programs;
- results of nonclinical and clinical trials, or the addition or termination of clinical trials or funding support by us, or existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any future product candidates receive regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- regulatory developments affecting any future product candidates or those of our competitors; and
- changes in general market and macroeconomic conditions.

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 common stock to fluctuate substantially. We believe that quarterly comparisons of our financial results should not be relied upon as an indication of our future performance.

Our cash and cash equivalents could be adversely affected if the financial institutions in which we hold our cash and cash equivalents fail.

We regularly maintain cash balances at third-party financial institutions, including formerly with Silicon Valley Bank, in excess of the FDIC insurance limit and similar regulatory insurance limits outside the United States. Further, if we enter into a credit, loan or other similar facility with a financial institution, certain covenants included in such facility may require as security that we keep a significant portion of our cash with the institution providing such facility. If a depository institution where we maintain deposits fails or is subject to adverse conditions in the financial or credit markets, we may not be able to recover all, if any, of our deposits, which could adversely impact our operating liquidity and financial performance.

Risks Related to Commercialization of Trudhesa and Any Future Product Candidates

Our future commercial success depends upon attaining significant market acceptance of Trudhesa and any future product candidates, if approved, among physicians, patients, health care payors and others in the medical community necessary for commercial success.

Trudhesa, and any product candidates for which we receive regulatory approval in the future may not gain market acceptance among physicians, health care payors, patients and the medical community. There are several approved acute treatments for migraine currently on the market, including triptans, calcitonin gene-related peptides antagonists, or gepants, lasmiditan and alternative formulations of DHE, such as Migranal, which is also administered intranasally. All of these are competitive with Trudhesa and our level of market acceptance of Trudhesa for the acute treatment for migraine may be lower than we expect. Market acceptance of Trudhesa or any other approved product candidates depends on a number of factors, including:

- the efficacy and safety of Trudhesa and any future product candidates;
- perceived advantages of Trudhesa and any future product candidates over alternative treatments, such as oral, IM and IV formulations;
- the indications for which the product candidates are approved and the labeling approved by regulatory authorities for use with the product candidates, including any warnings, limitations or contraindications contained in a product's approved labeling;
- acceptance by physicians and patients of Trudhesa and any future product candidate as a safe and effective treatment;
- the cost, safety and efficacy of treatment in relation to alternative treatments, including generic versions of the product candidates;
- the extent to which Trudhesa and any future product candidates are included on formularies of hospitals and managed care organizations;
- the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities for Trudhesa and any future product candidates;
- relative convenience and ease of administration of Trudhesa and any future product candidates;
- the prevalence and severity of adverse side effects;
- the timing of market introduction of competitive products;
- restrictions on the distribution of Trudhesa and any future product candidates;
- the effectiveness of our sales and marketing efforts;
- unfavorable publicity relating to Trudhesa and any future product candidates; and
- the approval of other new therapies for the same indications.

Market acceptance is critical to our ability to generate significant revenue and become profitable. Trudhesa and any other product candidate that is approved and commercialized, may be accepted in only limited capacities or not at all. If Trudhesa or any other approved product candidates are not accepted by the market to the extent that we expect, we may not be able to generate significant revenue and our business would suffer.

The market for Trudhesa may not be as large as we expect and, as a result, our product revenues may be lower than expected and our stock price may decline.

Our estimates of the potential market opportunity for Trudhesa include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys, including surveys commissioned by us. These assumptions include the size of our target populations, the prevalence and incidence of addressable migraines, the number of patients receiving current treatment, the percentage of patients unsatisfied with the current treatments, the number of diagnosed but untreated patients, the compliance and adherence of patients in our target populations, the number of treatment centers and prescribing physicians and the percentage of payer acceptance. While we believe that our internal assumptions are reasonable, if any of these assumptions proves to be inaccurate, then the actual market could be smaller

than our estimates of our potential market opportunity. If the actual market for Trudhesa is smaller than we expect, our product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability.

In addition, the FDA has required labeling restrictions for patients and uses of Trudhesa and we anticipate may require similar labeling restrictions for any future product candidates that may be approved by the FDA, including but not limited to contraindications for use in certain populations. For example, upper nasal space drug delivery may not be appropriate for use by patients with certain pre-existing conditions, such as chronic rhinitis with or without nasal polyposis or anatomical nasal obstruction.

If we are unable to maintain and expand commercial distribution capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We may expand our sales and marketing infrastructure for Trudhesa to further penetrate the migraine acute treatment market with Trudhesa or by marketing any future product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and retaining a sales force is expensive and time consuming and challenges could impact the trajectory and performance of a product.

Factors that may inhibit our efforts to commercialize Trudhesa and any future product candidates, if approved, on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any product candidates;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors for any future product candidates;
- restricted or closed distribution channels that make it difficult to distribute any future product candidates to segments of the patient population;
- the lack of complementary product candidates to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute any future product candidates outside of the United States or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market any future product candidates effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing any future product candidates.

Problems related to large-scale commercial manufacturing could cause delays in product launches, an increase in costs or shortages of Trudhesa and any future product candidates.

Manufacturing finished drug products, especially in large quantities, is complex. The commercialization of Trudhesa requires several manufacturing steps and involves complex techniques to assure quality and sufficient quantity, especially as the manufacturing scale increases. Additionally, if any future product candidates receive regulatory approval, they will also require several manufacturing steps and may involve complex techniques to assure quality and sufficient quantity, especially as the manufacturing scale increases. Trudhesa and any future product candidates will need to be made consistently and in compliance with a clearly defined manufacturing process pursuant to FDA regulations. Accordingly, it will be essential to be able to validate and control the manufacturing process to assure that it is reproducible. Slight deviations anywhere in the manufacturing process, including obtaining materials, filling, labeling, packaging, storage, shipping, quality control and testing, may result in lot failures, delay in the release of lots, product recalls or spoilage. Success rates can vary dramatically at different stages of the manufacturing process, which can lower yields and increase costs. We may experience deviations in the manufacturing process that may take significant time and resources to resolve and, if unresolved, may affect manufacturing output and cause us to fail to satisfy contractual commitments, lead to delays in our clinical trials or result in litigation or regulatory action. Such actions would hinder our ability to meet contractual obligations and could cause material adverse consequences for our business.

Reimbursement for any approved products may be limited or unavailable, which could make it difficult for us to sell Trudhesa or any future product candidates profitably.

In both domestic and foreign markets, sales of Trudhesa and any future product candidates, if approved, will depend, in part, on the extent to which the costs of any future product candidates will be covered by third-party payors, such as government health care programs, commercial insurance and managed health care organizations. These third-party payors decide which drugs will be covered and establish reimbursement levels for those drugs. The containment of health care costs has become a priority of foreign and domestic governments as well as private third-party payors. The prices of drugs have been a focus in this effort. Governments and private third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell any approved products profitably. Cost-control initiatives could cause us to decrease the price we might establish for any approved products, which could result in lower than anticipated product revenues.

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 relative to other alternatives, including generic products; and
- neither experimental nor investigational.

Adverse pricing limitations may hinder our ability to recoup our investment in historical and any future product candidates, even if such product candidates obtain marketing approval.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of any future product candidates to the payor. Further, there is significant uncertainty related to third-party payor coverage and reimbursement of newly approved product candidates, including any future product candidates if they are approved. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any future product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, Trudhesa and any future other product candidates. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any future product candidates. In addition, in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new product candidates. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved product candidates, which in turn will put pressure on pricing.

Price controls may be imposed in foreign markets, which may adversely affect our future profitability.

In some countries, including member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and other countries and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of any future product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any future product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

We face substantial competition, which may result in others discovering, developing or commercializing product candidates before, or more successfully, than we do.

The development and commercialization of new and improved pharmaceutical products is highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and

research organizations actively engaged in research and development of product candidates which may target the same markets as Trudhesa or any future product candidates. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of any of our future product candidates within those markets. We expect any future product candidates we develop and commercialize on our own or with our strategic partners, if approved, to compete with existing and leading products in the market on the basis of, among other things, product efficacy and safety, time to market, price, extent of adverse side effects experienced and convenience of administration and drug delivery.

For Trudhesa we are aware of the several competing efforts. Approved acute treatments for migraine include triptans, gepants (such as ZavzpretTM and Nurtec® both commercialized by Pfizer Inc.), lasmiditan and alternative formulations of DHE, such as Migranal, which is administered intranasally. Some of these competitor products have been launched. Some of these competitors are also developing product candidates that utilize alternative routes of administration, including Amneal Pharmaceuticals, Inc., Satsuma Pharmaceuticals, Inc. and Zosano Pharma Corporation, whose product candidates use nasal pumps or other drug delivery technologies.

One or more of our competitors may utilize their expertise in other methods of pharmaceutical drug delivery to develop and obtain approval for upper nasal space delivery products that may compete with any of our future product candidates. These competitors may include Aegis, Optinose and other smaller pharmaceutical companies. Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we have had to date. Our ability to compete effectively will depend, in part, on the timing and scope of regulatory approvals for these product candidates, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position, the safety and effectiveness of any of our future product candidates, the ease with which any of our future product candidates can be administered and the extent to which patients accept relatively new routes of administration. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any product candidates we may develop. Competitive products may reduce the demand and price for any product candidates we develop, making them obsolete or noncompetitive before we recover the expense of developing and commercializing such product. Our competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

We rely entirely on third parties for the manufacturing of Trudhesa and any future product candidates that we develop for nonclinical studies and clinical trials and expect to continue to do so for commercialization. If we encounter difficulties in negotiating manufacturing and supply agreements with third-party manufacturers and suppliers of our POD device and the active ingredients in Trudhesa, and any future product candidates our ability to commercialize such product candidates, if approved, would be impaired.

We do not own any manufacturing facilities and have limited experience in drug development and commercial manufacturing. We currently rely, and expect to continue to rely, on a limited number of experienced personnel and contract manufacturing organizations, or CMOs, and suppliers, including in some cases single-source suppliers, who would assist in the production, assembly, test, validation, supply, storage and distribution of any future drug-device combination product candidates in our clinical trials, and we do not control their activities. While we have developmental and commercial supply agreements in place with some of our key suppliers, we may not be able to obtain terms that are favorable to us or enter into commercial manufacturing and supply agreements at all with other necessary third parties. If we are unable to enter into such agreements on commercially reasonable terms, our ability to commercialize Trudhesa and any future product candidates, if approved, would be impaired, and our business, financial condition and results of operations would be materially adversely affected.

If and when product sales for Trudhesa, or any future product candidates, if approved, grow, Trudhesa and any future product candidates will require production processes to be scaled up. We will be dependent on external manufacturers and suppliers to ensure that their manufacturing processes can be scaled up adequately such that we are able to supply the market. If any of our key suppliers are unable or unwilling to scale up production, our product candidates would be impaired, and our business, financial condition and results of operations would be materially adversely affected.

Additionally, we currently have no plans to build our own clinical or commercial scale manufacturing facility. Should any of our product candidates receive approval, we would lack the resources and expertise to manufacture and test, on a commercial scale, the technical performance of our POD device and the active ingredients, and would need to incur significant expense to develop and acquire such expertise internally or partner with a third-party who possesses such expertise.

We rely on third parties to conduct nonclinical studies and clinical trials, and if they do not properly and successfully perform their obligations to do so, we may not be able to obtain regulatory approvals for any future product candidates.

We rely on contract research organization, or CROs and other third parties to assist in managing, monitoring and otherwise carrying out nonclinical and clinical trials for product candidates. We compete with many other companies for the resources of these third parties. Any disruption in supply from any supplier or manufacturing location, including on account of the COVID-19 pandemic, could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects. Further, the third parties on whom we rely generally may terminate their engagements at any time. Having to enter into alternative arrangements would delay development and commercialization of any future product candidates.

The FDA and comparable foreign regulatory authorities require compliance with regulations and standards, including GCP, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct many of our clinical trials, they are not our employees, and we are responsible for ensuring that each of these clinical trials is conducted in accordance with our general investigational plan, protocol and other requirements. Our reliance on these third parties for clinical research and development activities will reduce our control over these activities but will not relieve us of our responsibilities.

If these third parties do not successfully carry out their duties under their agreements, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of any future product candidates may not meet regulatory requirements. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our nonclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of any future product candidates on a timely basis, or at all.

If we encounter issues with our CMOs or suppliers, we may need to qualify alternative manufacturers or suppliers, which could impair our ability to sufficiently and timely manufacture and supply product candidates.

We currently depend, and have historically depended, on third parties to manufacture and supply our POD device, the active pharmaceutical ingredients and final formulations in our product candidates. Although we could obtain each of these components from other third-party suppliers, we would need to qualify and obtain FDA approval for another contract manufacturer or supplier as an alternative source for each such component, which could be costly and cause significant delays. Each of our current manufacturing and supply agreements include limitations on our ability to utilize alternative manufacturers or suppliers during the terms of the agreements, which impairs our ability to prepare in advance for any future manufacturing and supply shortages or quality issues.

In addition, some of our suppliers conduct their manufacturing operations for us at a single facility. Unless and until we qualify additional facilities, we may face limitations in our ability to respond to manufacturing and supply issues. For example, if regulatory, manufacturing or other problems require one of these manufacturers or suppliers to discontinue production at their respective facility, or if the equipment used for the production of our POD device or the active ingredients in these facilities is significantly damaged or destroyed by fire, flood, earthquake, power loss or similar events, the ability of such manufacturer or supplier to provide components or the active pharmaceutical ingredients needed for our product candidates, or to manufacture our product candidates may be significantly impaired. In the event that these parties suffer a temporary or protracted loss at their facility of our equipment, we would still be required to obtain FDA approval to qualify a new manufacturer or supplier, as applicable, as an alternate manufacturer or source for the respective component before any components manufactured by such manufacturer or by such supplier could be sold or used. To do so, we would need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidates according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize any of our approved products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture the product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies before implementing the change for our clinical supply for use in clinical trials or for commercial supply of any approved product. We may be unsuccessful in demonstrating the comparability of supplies before and after a manufacturing change, which could require the conduct of additional clinical trials and result in a delay or disruption in our clinical development plan or our ability to commercialize any approved product.

Any production shortfall that impairs the supply of our POD device or the active ingredients or any of these components could negatively impact our ability to complete clinical trials, obtain regulatory approval and commercialize future product candidates. If our future product candidates receive approval, a product shortfall could have a material adverse effect on our business, financial condition and results of operations and adversely affect our ability to satisfy demand for any future product candidates, which could materially and adversely affect our product sales and operating results.

If third-party manufacturers, wholesalers and distributors fail to perform as expected, or fail to devote sufficient time and resources to future product candidates, our clinical development may be delayed, our costs may be higher than expected or future product candidates may fail to be approved.

Our reliance on third-party manufacturers, wholesalers and distributors exposes us to the following risks, any of which could delay FDA approval of future product candidates and commercialization of such product candidates, result in higher costs, or deprive us of potential product revenues:

- our CMOs, or other third parties we rely on, may encounter difficulties in achieving the volume of production needed to satisfy commercial demand, may experience technical issues that impact quality or compliance with applicable and strictly enforced regulations governing the manufacture of pharmaceutical products, and may experience shortages of qualified personnel to adequately staff production operations;
- our wholesalers and distributors could become unable to sell and deliver future product candidates for regulatory, compliance and other reasons;
- our CMOs, wholesalers and distributors could breach or default on their agreements with us to meet our requirements for commercialization of future product candidates;
- our CMOs, wholesalers and distributors may not perform as agreed or may not remain in business for the time required to successfully produce, store, sell and distribute future product candidates and we may incur additional cost;
- our CMOs, wholesalers and distributors may misappropriate our proprietary information; and
- if our CMOs, wholesalers and distributors were to terminate our arrangements or fail to meet their contractual obligations, we may be forced to delay our commercial programs.

For example, we identified increased levels of impurities in some drug vials of certain drug lots used in our Trudhesa STOP 301 trial. Vials from those drug lots were removed from the trial and we conducted a root cause investigation, identifying the likely root cause as long stoppages in the production of two lots. If we encounter similar or other issues in connection with our commercial manufacturing of Trudhesa, we may face delays and shortages in production of Trudhesa, impacting our ability to fill prescriptions, and may face further scrutiny from the SEC.

Our reliance on third parties also reduces our control over any future product candidate development activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards. For example, the FDA and other regulatory authorities require that product candidates and any products that we may eventually commercialize be manufactured according to cGMP and QSR, and similar foreign standards. Any failure by our third-party manufacturers to comply with cGMP or QSR or maintain a compliance status acceptable to the FDA or other regulatory authorities or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any future product candidates. In addition, our third-party manufacturers will be subject to periodic inspections by the FDA and other regulatory authorities, and failure to comply with cGMP or QSR could be the basis for the FDA to issue a warning or untitled letter, withdraw approvals for product candidates previously granted to us, or take other regulatory or legal action, including request a recall or seize product candidates, total or partial suspension of production, suspension of clinical trials, refusal to approve pending applications or supplemental applications, detention of product, refusal to permit the import or export of product candidates, injunction, imposing civil penalties or pursuing criminal prosecution.

Additionally, if we scale up manufacturing of future product candidates and conduct required stability testing, issues may arise involving product-packaging and third-party equipment malfunctions. These issues may require refinement or resolution in order to proceed with commercial marketing of any future product candidates. In addition, quality issues may arise during scale-up and validation of commercial manufacturing processes. Any issues in our product or delivery devices could result in increased scrutiny by regulatory authorities, delays in our regulatory approval process, increases in our operating expenses, or failure to obtain or maintain approval for any future product candidates.

We may not be successful in establishing and maintaining strategic partnerships, which could adversely affect our ability to develop and commercialize product candidates, negatively impacting our operating results.

We continue to strategically evaluate and, as deemed appropriate, we may enter into partnerships in the future when strategically attractive, including potentially with major biotechnology or pharmaceutical companies, although there is no guarantee we will be able to enter into these agreements if we elect to do so. We face significant competition in seeking appropriate partners for any future product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully identify and work with partners, potential partners must view any future product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available product candidates for licensing by other companies. Even if we are successful in our efforts to establish strategic partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into strategic partnership agreements related to future product candidates could delay the development and commercialization of such candidates and reduce their competitiveness even if they reach the market. In addition, we have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market future product candidates effectively or create sufficient sales.

If we fail to establish and maintain strategic partnerships related to any future product candidates, we will bear all of the risk and costs related to the development of any such candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise, such as regulatory expertise, for which we have not budgeted. This could negatively affect the development of any unpartnered product candidate.

Risks Related to Regulatory Review and Approval of Product Candidates

The development and commercialization of pharmaceutical products is subject to extensive regulation, and we may not obtain regulatory approvals for INP105 or any other additional product candidates.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing, distribution, adverse event reporting, including the submission of safety and other post-marketing information and reports, and other possible activities relating to product candidate development, as well as any other product candidate that we may develop in the future, are subject to extensive regulation. Marketing approval of drugs in the United States requires the submission of an NDA to the FDA, and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, CMC, and cGMP at the manufacturing facilities. Further, product candidates must be approved by comparable regulatory authorities in other jurisdictions where we intend to market any future product candidates prior to commercialization.

FDA approval of an NDA is not guaranteed, and review and approval is an expensive and uncertain process that may take several years. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, there can be no assurance that any future product candidates will receive regulatory approval in the United States, or other jurisdictions. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for NDA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. We intend to seek FDA approval for any future product candidates through the Section 505(b)(2) regulatory pathway. If the FDA does not agree that the 505(b)(2) regulatory pathway is appropriate or scientifically justified for one or more future product candidates, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval.

Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits, and failure in clinical trials can occur at any stage. Companies in the pharmaceutical industry frequently suffer setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may further delay, limit or prevent marketing approval.

The FDA could delay, limit or deny approval of a product candidate for many reasons, including because the FDA:

- may not deem the product candidate to be safe and effective;

- determines that the product candidate does not have an acceptable benefit-risk profile;
- may not agree that the data collected from preclinical studies and clinical trials are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and may impose requirements for additional preclinical studies or clinical trials;
- may determine that adverse events experienced by participants in our clinical trials represent an unacceptable level of risk;
- may determine that population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- may disagree regarding the formulation, labeling and/or the specifications;
- may not approve the manufacturing processes associated with any future product candidate or may determine that a manufacturing facility does not have an acceptable compliance status;
- may conclude there are CMC issues that preclude approval of the NDA;
- may conclude that the drug substance or drug product manufacturing process is not in a state of control or does not meet cGMPs or all the regulatory requirements;
- may change approval policies or adopt new regulations; or
- may not accept a file for submission due to, among other reasons, the content or formatting of the submission.

We have only obtained FDA approval for Trudhesa to date. This relative lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for any future clinical product candidates. If we experience delays in obtaining approval of any future product candidates, our commercial prospects will be harmed and our ability to generate revenues will be materially impaired which would adversely affect our business, prospects, financial condition and results of operations.

Clinical failure may occur at any stage of clinical development, and we may never succeed in developing marketable product candidates or generating product revenue.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct clinical trials to demonstrate the safety and efficacy of any future product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing.

Any future NDA submissions may propose to bridge Listed Drugs, or LDs, for which we have conducted a comparative bioavailability study. The approval of Trudhesa or our prior clinical results for prior product candidates are not necessarily indicative of our ability to bridge to LD for future product candidates, as there can be significant variability in results between different clinical trials due to numerous factors, including the pharmacokinetics or pharmacodynamics of different drugs, changes in trial procedures, differences in the size and type of patient populations, including across geographies, changes in and adherence to the clinical trial protocols, and the rate of dropout among clinical trial participants. If we are not able to establish a bridge between a product candidate and each LD upon which it relies to demonstrate that such reliance is justified, we may be required to show safety and efficacy through one or more clinical trials. In addition, the long-term safety studies we are conducting or plan to conduct may reveal safety concerns, including with regard to nasal mucosa or olfactory function. If either or both of these outcomes occur, we may be prevented or delayed in obtaining marketing approval.

We may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on our distribution, such as in the form of a Risk Evaluation and Mitigation Strategy, or REMS. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would materially and adversely affect our business, results of operations and financial condition.

Delays in the commencement, enrollment or completion of clinical trials of any future product candidates, or in acceptance of foreign clinical trial data, could result in increased costs to us as well as a delay or failure in obtaining regulatory approval, or prevent us from commercializing future product candidates on a timely basis, or at all.

Any of our future clinical trials may not be conducted as planned or completed on schedule, if at all. For example, in February 2023 we announced a strategic reprioritization that included halting research and development efforts for our

product candidate INP105. A failure of one or more clinical trials can occur at any stage. Events that may prevent successful or timely commencement, enrollment or completion of clinical development include:

- changes in funding priorities that may result in delays or postponements of active clinical trials and development programs;
- delays by us in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining required IRB approval at each clinical trial site;
- delays in recruiting suitable patients to participate in clinical trials;
- the effects of COVID-19 on our ability to recruit and retain patients, including as a result of potential heightened exposure to COVID-19, prioritization of hospital resources toward the outbreak and unwillingness by patients to enroll or comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services;
- imposition of a clinical hold by regulatory agencies for any reason, including safety concerns or after an inspection of clinical operations or trial sites;
- failure by CROs, other third parties or us to adhere to clinical trial requirements;
- failure to perform clinical trials in accordance with the FDA's GCP or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays caused by patients not completing participation in a trial or not returning for post-treatment follow-up, which we have experienced and believe may be caused by patients experiencing reduced symptoms or incidences of disease;
- clinical trial sites or patients dropping out of a trial;
- delays or interruptions to supply or failure to ensure compliance with cGMP or quality standards of any future product candidates or the other product candidates in a combination product trial or other materials necessary to conduct clinical trials of any of our future product candidates;
- occurrence of adverse events in clinical trials that are associated with the product candidates that are viewed to outweigh their potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Delays, including delays caused by any of the above factors, can be costly and could negatively affect our ability to complete a clinical trial. If we are not able to successfully complete clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize future product candidates.

If we are not able to use the 505(b)(2) regulatory approval pathway for regulatory approval of any of our future product candidates or if the FDA requires additional clinical or nonclinical data to support an NDA under Section 505(b)(2) than we have previously anticipated, it will likely take significantly longer, cost significantly more and be significantly more complicated to gain FDA approval for future product candidates, and in any case may not be successful.

We intend to seek FDA approval for any future product candidates through the Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the Federal Food, Drug, and Cosmetic Act, or the FDCA. In general, Section 505(b)(2) allows a 505(b)(2) applicant to rely on the FDA's finding of safety or effectiveness for an LD only to the extent that the proposed product in the 505(b)(2) application shares common characteristics with the LD. The 505(b)(2) application must include sufficient data to support differences between the LD and the proposed drug in the 505(b)(2) application. If the FDA does not agree that the 505(b)(2) regulatory pathway is appropriate or scientifically justified for one or more of our future product candidates, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. For example, the FDA may not agree that we have provided a scientific bridge, through, for example, comparative bioavailability data, to demonstrate that reliance on the prior findings of safety or efficacy for an LD is justified. If we are unable to pursue a Section 505(b)(2) pathway, the time and financial resources required to obtain FDA approval for future product candidates would likely increase substantially. Moreover, the inability to pursue the Section

505(b)(2) regulatory pathway could result in new competitive products reaching the market before any of our future product candidates, which could materially adversely impact our competitive position and prospects.

Even though Trudhesa was approved through the Section 505(b)(2) regulatory pathway, we cannot assure you that nonclinical studies or clinical trials that we have conducted or that we currently anticipate conducting will be sufficient for approval or that we will receive the requisite or timely approvals for commercialization of any future product candidate. Although the Section 505(b)(2) pathway allows us to rely in part on the FDA's prior findings of safety or efficacy for approved LDs or on published literature, the FDA may determine that prior findings by the FDA or the published literature that we believe supports the safety or efficacy of one or more of our future product candidates is insufficient or not applicable to our application or that additional studies will need to be conducted. To the extent that we are relying on the Section 505(b)(2) regulatory pathway based on the approval of an LD for a similar indication, the FDA may require that we include in the labeling of such our other future product candidates, if approved, some or all of the safety information that is included in the labeling of the approved LD. Our approved labeling for Trudhesa includes the safety information included in the labeling of the approved LD used for our Trudhesa NDA, as well as the efficacy information for the LD, including a boxed warning. Moreover, even if future product candidates are approved through the Section 505(b)(2) regulatory pathway, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Our marketed product utilizes, and any future product candidates would utilize, similar drug delivery devices. If a drug delivery device in a future clinical trial demonstrates unanticipated biocompatibility, usability, performance or safety issues in a clinical or nonclinical study for one product candidate, our entire pipeline may be adversely affected.

Our marketed product and all of our prior product candidates utilize similar POD devices, which are designed to deliver the drug into the upper nasal space using a gas propellant. While our prior product candidates have been generally well tolerated in nonclinical studies and clinical trials, patients may in the future experience different or more severe adverse events due in part to our POD device. Any failure of our POD device to demonstrate adequate biocompatibility, usability, performance or safety could adversely affect the development, approval, or commercialization of Trudhesa or any future product candidates utilizing the same or similar POD device, including a suspension or delay of all ongoing development for future product candidates, or our marketed product candidate.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of any future product candidates may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of nonclinical studies and clinical trials and the submission of regulatory filings. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to reach subsequent milestones, receive marketing approval or commercialize future product candidates, including:

- the FDA and other governmental health authorities, IRBs, or ethics committees may not authorize or may delay authorizing us or our investigators to commence or continue a clinical trial or conduct a clinical trial at all or at a prospective trial site, such as by requiring us to conduct additional nonclinical studies and submit additional data or imposing other requirements before permitting us to initiate or continue a clinical trial;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of any future product candidates may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct nonclinical studies in addition to those we currently have planned or additional clinical trials or we may decide to abandon drug development programs for future product candidates;
- the number of patients required for clinical trials of future product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our contractors, such as our CROs, clinical trial sites or investigators, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that, we or our investigators, suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to health risks;
- the cost of planned clinical trials of future product candidates may be greater than we anticipate;
- the supply or quality of future product candidates or other materials necessary to conduct clinical trials of future product candidates may be insufficient or inadequate;
- our third-party suppliers, such as our contract manufacturers of the POD device and our active ingredients, may not provide us with the information we need for our marketing submissions or may not manufacture product for us that is in compliance with regulatory requirements; and
- any future product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from nonclinical or clinical testing of studies conducted by competitors that raise safety or efficacy concerns broadly about our POD technology, upper nasal space delivery or about any future product candidates specifically.

Clinical development, regulatory review and approval by the FDA and comparable foreign authorities are lengthy, time consuming, costly, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, future business will be substantially harmed.

Our marketed product and any future product candidates are subject to extensive governmental regulation relating to, among other things, development, clinical trials, manufacturing and commercialization. In order to obtain regulatory approval for the commercial sale of any future product candidates, we must demonstrate through extensive nonclinical studies and clinical trials that the candidate is safe and effective for use in each target indication.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the acceptance of clinical data developed in foreign geographies. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve a product candidate. We have only obtained regulatory approval for one product candidate, and it is possible that none of our future product candidates we may seek to develop will ever obtain regulatory approval. In addition, we may gain regulatory approval in some but not all of the territories available or some but not all of the target indications, resulting in limited commercial opportunity for the approved product.

Applications for any future product candidates could be delayed or could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies clinical trials or may refuse to accept data from nonclinical studies or clinical trials conducted in other geographies or jurisdictions;
- data collected from clinical trials may not be sufficient to support the submission of an NDA, or other submission, or to obtain regulatory approval in the United States or elsewhere;
- the FDA may determine that we cannot rely on the Section 505(b)(2) approval pathway for any future product candidates, in which case we may be required to conduct additional clinical trials, provide additional data and information and meet additional standards for product approval, resulting in increased time and financial resources required to obtain FDA approval for future product candidates;
- the FDA may determine that we have identified the wrong LD or LDs or that approval of a Section 505(b)(2) application for any future product candidates is blocked by patent or non-patent exclusivity of the LD or LDs;

- the FDA may require us to conduct additional clinical trials depending on the safety or exploratory efficacy data from our existing and planned future clinical trials;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for our proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications of third-party manufacturers with which we contract for clinical and commercial supplies;
- we or any third-party manufacturers may be unable to demonstrate compliance with cGMP to the satisfaction of the FDA or comparable foreign regulatory authorities, which could result in delays in regulatory approval or require us to withdraw or recall product candidates and interrupt commercial supply of any future product candidates; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any future product candidates, which would significantly harm our business, results of operations, and prospects.

Inadequate funding for the FDA, the SEC and other government agencies or other disruptions at these agencies could hinder these agencies' ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner 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. In addition, government funding of the SEC and 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, over the last several years, the U.S. government has shut down several times, and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. 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, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Results of earlier studies or clinical trials may not be predictive of future clinical trial results, and initial studies or clinical trials may not establish an adequate safety or efficacy profile for any future product candidates to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical and preclinical studies and early clinical trials may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. The results of preclinical studies and clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size, demographics and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial procedures and the rate of dropout among clinical trial participants. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of future product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell

these product candidates. Our failure to obtain marketing approval for any future product candidates would substantially harm our business, prospects, financial condition and results of operations.

Additionally, planned clinical trials may utilize an "open-label" trial design, as did our STOP 301 trial for Trudhesa. An "open-label" clinical trial is one where both the patient and investigator know that the patient is receiving the investigational product candidate. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware that patients have received treatment and may interpret the information collected more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our future product candidates in clinical trials when studied in a controlled environment with a double-blind placebo or active control.

Our future product candidates may cause undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by any future product candidates could cause us, or regulatory authorities, to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. Adverse events deemed to be caused by any future product candidates could have a material adverse effect on the development of any future product candidates and our business as a whole. For example, the most common adverse events in our STOP 301 trial evaluating Trudhesa included nasal congestion, nausea, nasal discomfort and unpleasant taste. Moreover, we could in the future observe local toxicity in the nasal or olfactory epithelia.

If we or others identify undesirable side effects caused by any future product candidates either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- we may be unable to obtain regulatory approval for future product candidates;
- our clinical trials may be put on hold;
- regulatory authorities may withdraw approvals of future product candidates or require additional nonclinical studies or clinical trials;
- regulatory authorities may require additional warnings in the labeling;
- regulatory authorities may require us to implement a REMS;
- a medication guide outlining the risks of such side effects for distribution to patients may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any future product candidates and could substantially increase commercialization costs.

Some of our clinical trials for our prior product candidates have been, and we may in the future conduct clinical trials for future product candidates, outside the United States, and the FDA or comparable foreign regulatory authorities may not accept data from such trials.

Some of our clinical trials for our prior product candidates have been conducted, and we may in the future choose to conduct one or more clinical trials, outside the United States. The acceptance of trial data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, the European Medicines Agency, or EMA, or any comparable foreign regulatory authority will accept data from trials conducted outside of

the United States or the applicable jurisdiction. If the FDA, EMA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of any future product candidates, which would significantly harm our business, results of operations, and prospects.

If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market any future product candidates in those jurisdictions.

We intend to market Trudhesa and any future product candidates, if approved, in international markets either directly or through partnerships. Such marketing will require separate regulatory approvals in each jurisdiction and compliance with numerous and varying regulatory requirements. The approval procedures vary from jurisdiction to jurisdiction and may require additional testing that we are not required to perform to obtain regulatory approval in the United States. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not guarantee approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not guarantee approval by regulatory authorities in other foreign jurisdictions or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize any future product candidates in any foreign market. If we or any future partner are unable to obtain regulatory approval for any future product candidates in one or more significant foreign jurisdictions, then the commercial opportunity for any future product candidates, as well as our financial condition, will be adversely affected.

Even if we receive regulatory approval for any future product candidates, they will be subject to ongoing regulatory requirements, which may result in significant additional expenses. Additionally, Trudhesa and any future product candidates, if approved, could be subject to labeling and other restrictions, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any future product candidates.

Any regulatory approvals that we receive for Trudhesa and any future product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed, or to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor safety and efficacy. For example, under the Pediatric Research Equity Act, we are required to conduct certain juvenile animal and pediatric studies in accordance with the timelines set forth in our Trudhesa NDA approval letter. These studies will require significant resources. We cannot predict the outcome of these studies. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event, or AE, reporting, storage, advertising, promotion and recordkeeping for any approved product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, including reporting of certain adverse events, malfunctions, corrections and removals related to the POD device, registration, as well as continued compliance with cGMP for the drug products, the quality system regulation, or QSR, for medical devices and GCP for any clinical trials that we conduct post-approval.

Later discovery of previously unknown problems with an approved product, including AEs of unanticipated severity or frequency, or with manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- holds on clinical trials;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- revisions to the labeling, including limitation on approved uses or the imposition of additional warnings, contraindications or other safety information, including boxed warnings;

- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- fines, warning or untitled letters;
- refusal by the FDA to approve pending applications or supplements to approved applications submitted by us, or withdrawal of product approvals;
- product seizure or detention, or refusal to permit the import or export of product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any future product candidates. 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 abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or not able to maintain regulatory compliance, we may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

We may be subject to enforcement action by the FDA or other government agencies or competitor lawsuits or other claims, including litigation brought by the government, if we engage or are found to have engaged in improper promotion of our products.

Our promotional materials and training methods must comply with FDA and other applicable laws and regulations, including laws and regulations prohibiting marketing claims that promote the off-label use of our products or that omit material facts or make false or misleading statements about the safety or efficacy of our products. We are responsible for training our marketing and sales force not to promote any future product candidates for off-label uses, but healthcare providers may use our products off-label as the FDA does not restrict or regulate a physician's choice of treatment within the practice of medicine. The FDA also could conclude that a claim is misleading if it determines that there are inadequate nonclinical and/or clinical data supporting the claim, or if a claim fails to reveal material facts about the safety or efficacy of our products. If the FDA determines that our promotional labeling or advertising materials promote an off-label use or make false or misleading claims, it could request that we modify our promotional materials or training content or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fines and criminal penalties.

The FDA closely regulates the pre and post-approval marketing and promotion of drugs to ensure they are promoted and marketed in compliance with the FDCA and its implementing regulations and only for the approved indications and in a manner consistent with the approved labeling. For example, our labeling for Trudhesa does not include any of the data from the exploratory efficacy endpoints that we evaluated in our Phase 3 safety clinical trial or contain any efficacy claims based on the results of this study. If the FDA disagrees with our claims or approach to describing the efficacy results from any data deemed as unreliable or uninterpretable, including our exploratory efficacy analyses, in our promotional materials, it may take enforcement action against us. In addition, without conducting head-to-head clinical trials designed to investigate the clinical superiority of any future product candidates to marketed products, we would not be able to make any such claims in our promotional materials. The FDA imposes stringent restrictions on manufacturers' communications and promotion of their products, including specific restrictions for promotions of products with boxed warnings. If we promote any future product candidates in a manner inconsistent with the FDA-approved labeling or otherwise not in compliance with the FDCA or implementing regulations, we may be subject to enforcement action. Violations of the FDCA relating to improper promotion of prescription drugs may lead to warning letters, investigations, violations under federal and state healthcare fraud and abuse laws, including the False Claims Act, as well as state consumer protection laws.

It is also possible that other federal, state or foreign enforcement authorities might take action if they determine that our promotional or training materials promote an unapproved use or make false or misleading claims, which could result in significant fines or penalties. Although our policy is to refrain from statements that could be considered off-label promotion of our products or false or misleading claims, the FDA or another regulatory agency could disagree with the manner in which we advertise and promote our products. Violations of the FDCA may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws, which may lead to costly penalties and may adversely impact our business. Recent court decisions have impacted the FDA's enforcement activity regarding off-label promotion in light of First Amendment considerations; however, there are still significant risks in this area, in part due to the potential for False Claims Act exposure. Competitors may also object to our promotional claims, which could lead to trade complaints to FDA or other actions related to unfair competition.

Many companies have also faced government investigations or lawsuits by whistleblowers who bring a qui tam action under the False Claims Act on behalf of themselves and the government for a variety of alleged improper marketing activities. In addition, the government and private whistleblowers have pursued False Claims Act cases against pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved uses. If we are found to have improperly promoted our products, we may be subject to significant liability, including civil fines, criminal fines and penalties, civil damages, exclusion from federally funded healthcare programs and potential liability under the federal False Claims Act and any applicable state false claims act. In addition, we may incur liability from claims initiated under the Lanham Act or other federal and state unfair competition laws with respect to how our products are marketed and promoted. Furthermore, the off-label use of our products may increase the risk of product liability claims. The scope of potential liability with respect to any such claims, enforcement actions, or lawsuits is uncertain, and we cannot assure you that we will not receive claims from competitors or other third parties or be subject to enforcement actions in the future from regulatory agencies. Moreover, threatened or actual government enforcement actions or lawsuits by third parties could generate adverse publicity, which could decrease demand for our products and require that we devote substantial resources that could be used productively on other aspects of our business.

Our relationships with health care professionals, institutional providers, principal investigators, consultants, potential customers and third-party payors are, and will continue to be, subject, directly and indirectly, to federal and state health care fraud and abuse, false claims, marketing expenditure tracking and disclosure, government price reporting, and privacy, data protection and data security laws. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal and state health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Our business operations and activities may be directly or indirectly subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. If we obtain FDA approval for any of any future product candidates and begin commercializing those product candidates in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to laws of the federal government and state governments in which we conduct our business relating to privacy, data protection and data security with respect to patient information. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, 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 a federal health care program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from a federal health care program, such as Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, health care benefits, items or services relating to health care matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered health care providers, health plans, and health care clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;

- the federal physician self-referral law, commonly known as the Stark Law, which prohibits a physician from making a referral to an entity for certain designated health services reimbursed by Medicare or Medicaid if the physician or a member of the physician's family has a financial relationship with the entity, and which also prohibits the submission of any claims for reimbursement for designated health services furnished pursuant to a prohibited referral;
- the federal Physician Payments Sunshine Act, created under Section 6002 of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, or the ACA, and its implementing regulations require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, Centers for Medicare & Medicaid Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) physician assistants, certain types of advanced practice nurses, and teaching hospitals, including ownership and investment interests held by the physicians described above and their immediate family members, with the information made publicly available on a searchable website;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal government price reporting laws, changed by the ACA to, among other things, increase the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program and offer such rebates to additional populations, that require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on any future product candidates, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts);
- the Foreign Corrupt Practices Act, a United States law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals); and
- state law equivalents and adjuncts to many of the above federal laws, such as anti-kickback, false claims, consumer protection, unfair competition, and privacy and data security laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submission of claims involving any future product candidates or related health care services for reimbursement by any third-party payor, including public and commercial insurers; state laws that require biotech companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to health care providers; state laws that require drug manufacturers to file reports with states regarding marketing information, such as the tracking and reporting of gifts, compensation and other remuneration and items of value provided to health care professionals and entities (compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business or increase enforcement scrutiny of our activities); state laws regarding the reporting of certain pricing information; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, with differing effects and obligations.

In addition, the regulatory approval and commercialization of any future product candidates outside the United States will also likely subject us to foreign equivalents of the laws and regulations mentioned above, including reporting requirements detailing interactions with and payments to healthcare providers, and requirements in Europe and other jurisdictions relating to privacy, data protection and cybersecurity, among other foreign laws. In addition to health information privacy, data security, and data protection laws that apply to some of the patient data we hold, other privacy, data security and data protection laws may also apply to such data, as well as to the personal data of our employees and other individuals generally. Many of these laws governing privacy, data protection and cybersecurity differ from each other in significant ways and may not have the same effects or obligations, thus complicating compliance efforts. We expect to incur increased costs of compliance with such laws and regulations as they continue to evolve, as well as the increased risk of regulatory investigations, enforcement actions, and other claims and litigation, with the potential for significant fines, penalties, and other liabilities in the event of actual or alleged noncompliance. Any of these could adversely affect our business, financial condition, and results of operations.

The ACA, among other things, amended the intent standard of the federal Anti-Kickback Statute and criminal health care fraud statutes to a stricter standard such that a person or entity no longer needs to have actual knowledge of this

statute or specific intent to violate it. In addition, the ACA codified case law 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 federal False Claims Act.

Efforts to ensure that our business arrangements with third parties will comply with applicable health care laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other health care laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, imprisonment, loss of eligibility to obtain approvals from the FDA, qui tam actions, lawsuits, government investigations, exclusion from participation in government contracting, healthcare reimbursement, or other federal or state government healthcare programs, including Medicare and Medicaid, corporate integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

The impact of recent health care reform legislation and other changes in the health care industry and in healthcare spending on us is currently unknown, and may adversely affect our business model.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any future product candidates. 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 abroad. 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 lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs.

On September 9, 2021, the Biden administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The HHS plan includes, among other reform measures, proposals to lower prescription drug prices, including by allowing Medicare to negotiate prices and disincentivizing price increases, and to support market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase price transparency. These proposals recently culminated in the enactment of the IRA in August 2022, which will, among other things, allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in January 2023 for Medicare Part B and October 2022 for Medicare Part D, the IRA will also penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. The full economic impact of the IRA is unknown at this time, but the law's passage may affect the pricing of our products and product candidates. The adoption of restrictive price controls in new jurisdictions, more restrictive controls in existing jurisdictions or the failure to obtain or maintain timely or adequate pricing could also adversely impact revenue. We expect pricing pressures will continue globally.

At the state level, legislatures are increasingly passing legislation and implementing 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.

We expect that additional state and federal healthcare reform measures will be adopted in the future. Such reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize Trudhesa and any future product candidates if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are not able to obtain and enforce patent protection for our technologies or any future product candidates, development and commercialization of our technology and any future product candidates may be adversely affected.

Our success depends in part on our ability to obtain, maintain, protect and enforce patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, relating to any future product candidates, our technology such as our proprietary POD nasal drug delivery platform, and methods for treating patients using any future product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. Our patent portfolio as of February 1, 2022 contained 8 U.S. issued patents and 34 patents issued in ex-U.S. jurisdictions including Australia, Brazil, Canada, China, Switzerland, Germany, France, Great Britain, Japan, and Russia and 13 U.S. pending applications as well as 80 patent applications pending in ex-U.S. jurisdictions including Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, Korea, Mexico, New Zealand, Russia, South Africa and one pending international patent application that cover our marketed product candidates, historical product candidates, and our proprietary POD nasal drug delivery platform. We may not be able to apply for patents on certain aspects of our technology and any future product candidates in a timely fashion or at all. Further, we may not be able to prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of any patent applications that we license from third parties, or the ability to maintain the rights to patents licensed to third parties, and should we decide to license any of our patents to third parties in the future, we may not retain sufficient rights to prosecute and enforce such patents. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing product candidates and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our technology and any future product candidates or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely affect our position in the market.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary future product candidates and drug delivery system. Accordingly, despite our efforts, we may be unable to prevent third parties from infringing upon or misappropriating our intellectual property. While we will endeavor to try to protect our technology and future product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive and sometimes unpredictable. The failure to adequately protect our intellectual property and other proprietary rights could materially harm our business.

We may be required to spend significant resources to monitor and protect our intellectual property rights. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. Any patents that are issued may subsequently be invalidated or otherwise limited, allowing other companies to develop offerings that compete with our offerings, which could adversely affect our competitive business position, business prospects and financial condition. In addition, issuance of a patent does not guarantee that we have a right to practice the patented invention. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action before patent offices for a given period after allowance or grant, during which time third parties can raise objections against such initial grant, or in court. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our patents, trade secrets or other intellectual property. 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, intellectual property that is important to any future product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, and results of operations.

In addition, there can be no assurance that:

- others will not or may not be able to make, use or sell upper nasal space product candidates that are the same as or similar to any of our future product candidates but that are not covered by the claims of the patents that we own;
- we or our existing or future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own;
- we, or our existing or future collaborators, are the first to file patent applications covering certain aspects of our inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- a third party will not challenge our patents and, if challenged, a court would hold that our patents are valid, enforceable and infringed;
- any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties;
- we may develop additional proprietary technologies that are patentable;
- the patents of others will not have a material or adverse effect on our business, financial condition, results of operations and prospects; and
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

If we, our licensor or collaborators fail to maintain the patents and patent applications covering our technology or future product candidates, our competitors might be able to enter the market, which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for certain aspects of our technology and any future product candidates, we also consider trade secrets, including confidential and unpatented know-how, important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CMOs, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, we cannot be certain that such agreements have been entered into with all relevant parties. In addition, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Other companies or organizations may challenge our or our licensor's patent rights or may assert patent rights that prevent us from developing and commercializing any future product candidates.

The issued patents and pending patent applications in the United States and in key markets around the world that we own or license claim many different devices, compositions and methods, including processes relating to the discovery, development, manufacture and commercialization of upper nasal space drug delivery. As the field of upper nasal space drug delivery continues to mature, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue and, if they do, as to when, to whom, and with what claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material and adverse effect on our business, financial condition, results of operations and prospects or our ability to successfully compete.

We may not be able to protect our intellectual property rights throughout the world.

Obtaining a valid and enforceable issued or granted patent covering our technology in the United States and worldwide can be extremely costly, and our or our licensors' or collaborators' intellectual property rights may not exist in some countries outside the United States or may be less extensive in some countries than in the United States. In jurisdictions where we or our licensor or collaborators have not obtained patent protection, competitors may seek to use our or their technology to develop their own products and further, may export otherwise infringing products to territories where we or they have patent protection, but where it is more difficult to enforce a patent as compared to the United States. Competitor products may compete with our future product candidates in jurisdictions where we do not have issued or granted patents or where our or our licensors' or collaborators' issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly relating to pharmaceuticals. This could make it difficult for us or our licensor or collaborators to prevent the infringement of our or their patents or marketing of competing products in violation of our or their proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our and our licensor's or collaborators' efforts and attention from other aspects of our business, could put our and our licensor's or collaborators' patents at risk of being invalidated or interpreted narrowly, and our and our licensor's or collaborators' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensor or collaborators. We or our licensor or collaborators may not prevail in any lawsuits that we or our licensor or collaborators initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, various scopes of patent protection may be granted on the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensor or collaborators encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensor or collaborators are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business, financial condition, results of operations and prospects may be adversely affected.

We, our collaborators, or any future strategic partners may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our technology or any future product candidates, or put our patents and other proprietary rights at risk.

Competitors may infringe our patents or other intellectual property. If we were to initiate legal proceedings against a third party to enforce a patent covering one of any future product candidates or our technology, the defendant could counterclaim that our patent is 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, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that an individual connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a materially misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of any future product candidates or certain aspects of our platform technology. Such a loss of patent protection could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. 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 a material adverse effect on the price of our common stock. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

Intellectual property rights of third parties could adversely affect our ability to commercialize our technology or any future product candidates, and we, our licensor or collaborators, or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights. We might be required to litigate or obtain licenses from third parties in order to develop or market our technology or any future product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.

We, our collaborators, or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, post grant review and *inter partes* review proceedings before the USPTO, and corresponding foreign patent offices. We have previously received communications from third parties claiming that our technology infringes on their patents. While we do not believe that these claims have merit, we cannot be certain that these third parties would not pursue infringement claims against us. There are issued and pending patents that might claim aspects of our technology and any future product candidates, and modifications that we may need to apply to our technology or any future product candidates. Thus, it is possible that one or more individuals or organizations will hold patent rights to which we will need a license. If those individuals or organizations refuse to grant us a license to such patent rights or refuse to grant us a license on reasonable terms, we may not be able to market product candidates or perform research and development or other activities covered by these patents which could have a material and adverse effect on our business, financial condition, results of operations and prospects. We are obligated under certain of our license and collaboration agreements to indemnify and hold harmless our licensor or collaborators for damages arising from intellectual property infringement by us. If we, our licensor or collaborators, or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have infringed willfully. In addition, we, our licensor or collaborators, or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our existing or future collaborators may be unable to effectively market our technology or any future product candidates, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation could divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent

litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

Because the upper nasal space therapeutics landscape is still evolving, it is difficult to conclusively assess our freedom to operate without infringing on third-party rights. Our competitive position may suffer if patents issued to third parties or other third-party intellectual property rights cover our technology or any future product candidates or elements thereof, or our manufacture or uses relevant to our development plans. In such cases, we may not be in a position to develop or commercialize our technology or any future product candidates until such patents expire or unless we successfully pursue litigation to nullify or invalidate the third-party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms. There may be issued patents held by third parties of which we are not aware that, if found to be valid and enforceable, could be alleged to be infringed by our POD nasal drug delivery platform and related technologies and future product candidates. There also may be pending patent applications of which we are not aware that may result in issued patents, which could be alleged to be infringed by our POD nasal drug delivery platform and related technologies and future product candidates. If such an infringement claim should be brought and be successful, we may be required to pay substantial damages, including potentially treble damages and attorneys' fees for willful infringement, and we may be forced to abandon our technology or any future product candidates or seek a license from any patent holders. No assurances can be given that a license will be available on commercially reasonable terms, if at all.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering any future product candidates or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technology, any future product candidates or the use of any future product candidates. Third-party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing any future product candidates. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our technology or any future product candidates that are held to be infringing. We might, if possible, also be forced to redesign our technology or any future product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property rights of third parties could delay the development timeline with respect to one or more of our future product candidates.

Trudhesa includes a prior-approved formulation of our active pharmaceutical ingredient and certain of our prior product candidates include prior-approved active pharmaceutical ingredients. We are not aware of any unexpired patents that cover these active pharmaceutical ingredients, and there are no unexpired patents or regulatory exclusivities listed on the FDA Orange Book for the formulation we are using in Trudhesa. However, it is possible that one or more individuals or organizations will hold patent rights to which we will need to obtain a license. If those individuals or organizations refuse to grant us a license to such patent rights or refuse to grant us a license on commercially reasonable terms, our development timeline with respect to one or more future product candidates may be materially and adversely delayed.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. 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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may be subject to claims that we or our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or their former employers. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our technology or any future product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Patent terms may be inadequate to protect our competitive position on our technology or any future product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our technology or any future product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our products.

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 non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm or rely on our outside counsel to pay these fees due to the USPTO and non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance 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. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Changes in U.S. patent and ex-U.S. patent laws could diminish the value of patents in general, thereby impairing our ability to protect any future product candidates.

Changes in either the patent laws or interpretation of the patent laws in the United States or in other ex-U.S. jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. In the United States, numerous recent changes to the patent laws and proposed changes to the rules of the USPTO may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. For example, the decision by the U.S. Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence that is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we may develop product candidates that contain modifications that we believe are not found in nature. However, this decision has yet to be unambiguously interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. 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 decisions by the U.S. Congress, the federal courts and the USPTO, and similar legislative and regulatory bodies in other countries in which may pursue patent protection, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the U.S. transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. A third party that files a patent application in the USPTO after March 2013, but before we do, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the U.S. and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (i) file any patent application related to any future product candidates or (ii) invent any of the inventions claimed in our patents or patent applications. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents 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 a material adverse effect on our business, financial condition, and results of operations.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Employee Matters, Managing Growth and Other Risks Related to Our Business

We may be required to expand our operations capabilities in the future, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

While we recently conducted a reduction in force to reprioritize on Trudhesa, we may be required to expand our development, regulatory, manufacturing, marketing and sales capabilities in the future, or contract with third parties to

provide these capabilities for us, which could result in growth to the number of our employees and the scope of our operations, particularly in the area of commercialization, manufacturing and clinical strategy. Future growth will impose significant added responsibilities on members of our management. Our future financial performance and our ability to commercialize Trudhesa, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. Any expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop and commercialize any future product candidates.

We are highly dependent on members of our senior management, including Adrian Adams, our Chairman President and Chief Executive Officer, John Hoekman, Ph.D., Chief Technology and Development Officer and one of our founders, and Leonard S. Paolillo, our Chief Commercial Officer. Although we have entered into employment agreements with our executive officers, each of these persons may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees 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 any future product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key 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. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Further, the reduction in employee and non-employee expenses announced in February 2023 may also make retention of our current personnel both more important and more challenging. This reduction in workforce expenses resulted in the loss of longer-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel

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

As a public company, and particularly after we are no longer an emerging growth company, we will continue to incur significant legal, accounting and other expenses on an ongoing basis that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market, or Nasdaq, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We will need to hire additional accounting, finance and other personnel and make further investments in processes and systems in connection with these ongoing efforts. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements and future changes to such requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company or a non-accelerated filer, we will not be required to

include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Employees may also misappropriate information in violation of applicable insider trading laws, which could also seriously harm our reputation even if we are not deemed to be at fault. It is not always possible to identify and deter employee misconduct, 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. 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, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any future product candidates.

We face an inherent risk of product liability as a result of the commercial sale of Trudhesa and any other approved future product candidate, as well as from clinical testing of any future product candidates. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any future product candidates. Even a successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in:

- injury to our reputation;
- decreased demand for future product candidates or products that we may develop;
- withdrawal of clinical trial participants;
- costs to defend the related litigations;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals, or labeling, marketing or promotional restrictions;

- loss of revenue;
- the inability to successfully commercialize Trudhesa and any future product candidates, if approved; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of any future product candidates we develop. We currently carry product liability insurance covering the commercial sale of Trudhesa and our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, we could prevent or inhibit the development and commercial production and sale of any future product candidates, which could adversely affect our business, financial condition, and results of operations.

The security of the information technology systems used in our business may be compromised, and confidential information, including non-public personal information, could be improperly disclosed.

Our information technology systems, and those of our contractors, service providers and consultants, may be vulnerable to physical or electronic intrusions, computer viruses or other attacks, as well as employee, vendor, or contractor errors or malfeasance. As part of our business, we and our contractors and consultants maintain large amounts of confidential information, including non-public personal information on patients and our employees. Breaches in security and other information security events and incidents, including from ransomware, other malicious code, and other cyberattacks, could result in interruption to our systems and operations, or those of our contractors, consultants or our respective service providers, and the loss, unavailability, and unauthorized modification, use, acquisition or disclosure of information, including information subject to intellectual property protection or for which the loss or other compromise of such information may lead to the loss of intellectual property protection. Any such breach or other incident may result in significant costs to remediate and otherwise respond, including efforts to analyze, correct, eliminate, remediate or work around deficiencies in our systems or our security measures, recover and validate data, and to address any applicable legal or contractual obligations. Further, any actual or perceived breach in security or security incident may result in potential regulatory actions or litigation, including material claims for damages, interruption to our operations, delays in regulatory filings and approvals, damage to our reputation or otherwise have a material adverse effect on our business, financial condition and operating results. Like many businesses, we have been in the past, and may again be in the future, subject to phishing attacks. In 2018 we experienced a successful phishing attack. While we were able to swiftly contain and remediate this incident, without a material impact to our business, there can be no assurances that we will be able to defend against or successfully remediate any such attacks that may occur in the future. Further, companies have experienced an increase in phishing and social engineering attacks from third parties, including in connection with the COVID-19 pandemic. Also, due to the COVID-19 pandemic, the majority of our employees are working remotely as of December 31, 2022. As a result, we may have increased cybersecurity and data security risks, due to increased use of home wi-fi networks and virtual private networks, as well as increased disbursement of physical machines. While we have implemented IT controls to reduce the risk of a cybersecurity or data security breach or incident, there is no guarantee that these measures will be adequate to safeguard all systems, especially with an increased number of employees working remotely. While we expect to implement and maintain appropriate information security policies and systems in order to prevent unauthorized loss, unavailability, modification, use or disclosure of confidential information, including non-public personal information and other information relating to individuals, there can be no assurance that any such loss, unavailability, modification, use or disclosure will not occur. We incur significant costs in an effort to detect and prevent security breaches and other security-related incidents and we expect our costs will increase as we make improvements to our systems, policies and processes to prevent further breaches and incidents. In the event of a future breach or incident, we could be required to expend additional significant capital and other resources in an effort to prevent further breaches or incidents, which may require us to divert substantial resources. Moreover, we could be required or otherwise find it appropriate to expend significant capital and other resources to respond to, notify third parties of, and otherwise address the incident or breach and its root cause. Each of these could require us to divert substantial resources.

While we maintain insurance with respect to cybersecurity, our insurance may be insufficient to cover all liabilities incurred by us in connection with any privacy or cybersecurity incidents. We also cannot be certain that any insurance coverage will be adequate for data handling or data security liabilities actually incurred, that insurance will continue to be available to us on economically reasonable terms, or at all, or that any insurer will not deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence

of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could have a material adverse effect on our business, including our financial condition, operating results and reputation.

If we acquire complementary business or technologies in the future, we may be unable to integrate such acquired businesses and technologies successfully or fail to achieve the expected benefits.

Although we have not made any acquisitions to date, our business strategy in the future may include acquiring other complementary therapies, products, technologies or businesses. We also may enter into relationships with other businesses to expand our domestic and international operations. An acquisition, investment, or business relationship may result in unforeseen operating difficulties and expenditures. In particular, we may encounter difficulties assimilating or integrating the businesses, therapies, technologies, products, services, personnel or operations of the acquired companies, particularly if the key personnel of the acquired companies choose not to work for us. Acquisitions may also disrupt our business, divert our resources and require significant management attention that would otherwise be available for the development of our business. Moreover, the anticipated benefits of any acquisition, investment or business relationship may not be realized or we may be exposed to unknown liabilities.

Negotiating these transactions can be time consuming, difficult, and expensive, and our ability to close these transactions may often be subject to approvals that are beyond our control. Consequently, these transactions, even if undertaken and announced, may not close. Even if we do successfully complete acquisitions, we may not ultimately strengthen our competitive position or achieve our goals, and any acquisitions we complete could be viewed negatively by our customers, securities analysts and investors.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Unused losses incurred in taxable years beginning on or prior to December 31, 2017, will carry forward to offset future taxable income, if any, until such unused losses expire. Under the Tax Reform Act, as modified by the Coronavirus Aid, Relief and Economic Security Act, or the CARES Act, unused U.S. federal net operating losses generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely but the deductibility of such federal net operating losses is limited to 80% of current year taxable income in taxable years beginning after December 31, 2020. As a result, our net operating loss carryforwards generated in taxable years beginning on or before December 31, 2017, may expire prior to being used, and the deductibility of our net operating loss carryforwards generated in taxable years beginning after December 31, 2017 in taxable years beginning after December 31, 2020, may be limited. It is uncertain if and to what extent various states will conform to the Tax Reform Act or the CARES Act. In addition, both our current and our future unused losses and other tax attributes may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) if we undergo, or have undergone, an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a three-year period. We have not completed a Section 382 study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since our formation due to the complexity and cost associated with such a study and the fact that there may be additional ownership changes in the future. If we undergo an ownership change (or if we previously underwent such an ownership change), our ability to use all of our pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use all or a material portion of our net operating losses and other tax attributes, which could adversely affect our future cash flows.

Changes in U.S. tax law could adversely affect our financial condition and results of operations.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, the CARES Act was enacted, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Future changes in U.S. tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult

with their legal and tax advisors regarding the implications of potential changes in U.S. tax laws on an investment in our common stock.

The ongoing COVID-19 pandemic, or similar public health crises, could have a material adverse impact on our business, financial condition and results of operations, including through disruption to our planned clinical trials, supply chains, business operations and commercialization efforts for Trudhesa and any future product candidates.

The continued presence of the COVID-19 global pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services has fallen. The extent to which COVID-19 impacts our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, potential waves or cycles of the pandemic or new virus variants, and the actions to contain the virus or treat its impact. For example, ineffective or uncoordinated vaccine deployment in the future or other responses to COVID-19, the emergence of more virulent or infectious variants of the virus, or limitations on vaccine availability could risk increasing the duration and severity of the pandemic, which could have various negative impacts on our business, the extent of which we cannot fully predict.

Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis for our planned clinical trials may be delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. Additionally, some participants and clinical investigators may not be able to comply with clinical trial protocols. For example, quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we may be unable to conduct our planned clinical trials. If the global effort to control future resurgences of COVID-19 and treat COVID-19 patients is impeded for an extended period of time, we risk a delay in activating sites and enrolling subjects as previously projected. Any such delays to future clinical trials for any future product candidates could impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital earlier than we had previously planned. We may be unable to raise additional capital if and when needed, which may result in further delays or suspension of our development plans.

Further, as a result of the continued presence of the COVID-19 pandemic, we may in the future be required in the future to develop and implement additional clinical trial policies and procedures based on new guidance and regulatory requirements promulgated by the FDA or other regulatory authorities. A new resurgence of infections and deaths related to COVID-19 could also disrupt certain healthcare and healthcare regulatory systems globally. Such disruptions could continue divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially adversely affect the development and study of any future product candidates.

The ongoing COVID-19 pandemic could have an adverse impact on our commercialization efforts for Trudhesa due to future government-imposed quarantines, stay at home orders, travel restrictions, mandated business closures and other public health safety measures in response to rising infections and deaths which may result in limiting our ability to hire additional sales force resources, conduct necessary trainings of such sales force and attending and presenting at various conferences or other programs. Even though Trudhesa has been approved by the FDA, future government-imposed orders may also result in patients not visiting their healthcare providers or their pharmacies to get their prescriptions filled, in-person interactions by sales and medical representatives in healthcare settings may be suspended, and any remote interactions may be less effective than in-person interactions. These factors could have an adverse impact on our business and our ability to effectively commercialize Trudhesa.

We currently utilize third parties to, among other things, manufacture raw materials and any future product candidates, components, parts, and consumables, and to perform quality control and testing. If either we or any third-party in the supply chain for materials used in the production of any future product candidates are adversely impacted by restrictions resulting from the COVID-19 pandemic, our supply chain may be disrupted, limiting our ability to manufacture any future product candidates for our future clinical trials.

The ultimate impact of the current pandemic, or any other health epidemic, is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our planned clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Our Common Stock

The market price of our common stock may be volatile.

The market price of our common stock has been and may continue to be volatile. The market price for our common stock may be influenced by many factors, including the other risks described in this section and the following:

- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the life sciences and pharmaceutical sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for any future product candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- receipt of marketing approval for any future product candidates;
- results of nonclinical studies and clinical trials of any future product candidates, or those of our competitors or our existing or future collaborators;
- introductions and announcements of new product candidates by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to any future product candidates;
- material and adverse impact of the COVID-19 pandemic on the markets and the broader global economy;
- the success of competitive products or technologies;
- actions taken by regulatory agencies with respect to any future product candidates, clinical trials, manufacturing process or sales and marketing terms;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentration in ownership of our common stock;
- changes in accounting principles;
- potential litigation or the threat thereof;
- terrorist acts, acts of war or periods of widespread civil unrest;

- natural disasters and other calamities; and
- general economic, industry and market conditions.

In addition, the stock market in general, and the markets for pharmaceutical and medical device stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of these companies, including as a result of the COVID-19 pandemic. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

Our principal stockholders and management 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, 2022, our executive officers, directors and their respective affiliates owned a substantial portion of our voting stock. As a result, these stockholders, if acting together, have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an "emerging growth company" and we cannot be certain if the reduced reporting 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 Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, (ii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iii) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data in the annual reports.

We could be an emerging growth company until December 31, 2026, although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30, or if we have total annual gross revenue of $1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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 share price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period. Our financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an "emerging growth company" or affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-emerging growth companies and the date on which we will adopt the recently issued accounting standard.

Anti-takeover provisions in our restated certificate of incorporation and our restated bylaws and under Delaware or Washington law could make an acquisition of our business, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

Moreover, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Likewise, because our principal executive offices are located in Washington, the anti-takeover provisions of the Washington Business Corporation Act may apply to us under certain circumstances now or in the future. These provisions prohibit a "target corporation" from engaging in any of a broad range of business combinations with any stockholder constituting an "acquiring person" for a period of five years following the date on which the stockholder became an "acquiring person." Any of these provisions of our charter documents or Delaware or Washington law could, under certain circumstances, depress the market price of our common stock.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders and our restated bylaws designate federal district courts as the sole and exclusive forum for actions under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees, or agents.

Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under the DGCL: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision.

Our restated bylaws also provide that the federal district courts of the United States of America is the exclusive forum for the resolution of any complaint asserting a cause of action under the Securities Act. The enforceability of similar exclusive federal forum provisions in other companies' organizational documents has been challenged in legal proceedings, and while the Delaware Supreme Court has ruled that this type of exclusive federal forum provision is facially valid under Delaware

law, there is uncertainty as to whether other courts would enforce such provisions and that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation or restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, operating results and financial condition.

General Risk Factors

Natural disasters, catastrophic events and calamities including epidemics and pandemics may disrupt our business.

Natural disasters or other catastrophic events may damage or disrupt our operations and thus could harm our business. For example, our headquarters are located in Seattle, Washington, an earthquake-prone area. A natural disaster or catastrophic event in Seattle could interrupt our operations and impair access to internal systems, documents, and materials critical to the operation and growth of our business.

Further, occurrences of epidemics or pandemics, depending on their scale, may result in damage to the national and local economies within our geographic area. Global economic conditions may be disrupted by widespread outbreaks of infectious or contagious diseases, and such disruption may adversely affect clinical development plans. See "Risk Factors—The ongoing COVID-19 pandemic, or similar public health crises, could have a material adverse impact on our business, financial condition and results of operations, including the execution of our planned clinical trials."

As we grow, the need for business continuity planning and disaster recovery plans will become increasingly important. 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. If we are unable to develop adequate plans to ensure that our business functions continue to operate during and after a disaster, and successfully execute on those plans in the event of a disaster or emergency, our business could be harmed.

We and our CMOs must comply with environmental, health and safety laws and regulations, and failure to comply with these laws and regulations could expose us to significant costs or liabilities.

We and our CMOs are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the use, generation, manufacture, distribution, storage, handling, treatment, remediation and disposal of hazardous materials and wastes. Hazardous chemicals, including flammable and biological materials, are involved in certain aspects of our business, and we cannot eliminate the risk of injury or contamination from the use, generation, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials and wastes. In the event of contamination or injury, or failure to comply with environmental, health and safety laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources. We could also incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We are uninsured for third-party injury from contamination.

Environmental, health and safety laws and regulations are becoming increasingly more stringent. We may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our CMOs, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with any future product candidates, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of any future product candidates or products.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our common stock, our stock price and trading volume could decline.

The trading market for our common stock can be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our common stock could be impacted negatively. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our nonclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal executive office is located in Seattle, Washington, where we lease a total of approximately 11,568 square feet of office and laboratory space that we use for our administrative, research and development and other activities. Our lease expires in August 2024.

We also lease approximately 8,045 square feet of office space in Malvern, Pennsylvania, the lease term is 127 months, expecting to commence in the second quarter of 2023.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

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 for Common Stock

Our common stock began trading on the Nasdaq Global Market under the symbol "IMPL" on April 23, 2021. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of March 15, 2023, there were approximately 67 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividend Policy

We currently intend to retain all available funds and future earnings to fund the development and growth of our business and we do not anticipate paying any cash dividends in the foreseeable future.

Securities Authorized for Issuance under Equity Compensation Plans

See Part III, Item 12 of this report for information regarding securities authorized for issuance under our equity compensation plans

Recent Sales of Unregistered Securities

None.

Use of Proceeds from our Initial Public Offering of Common Stock

None

Purchases of Equity Securities By the Issuer and Affiliated Purchasers

None.

Item 6. [Reserved]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following management's discussion and analysis of financial condition and results of operations in conjunction with our consolidated financial statements and notes thereto included in Part II, Item 8 of this Annual Report on Form 10-K. This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section of this Annual Report on Form 10-K titled "Risk Factors" and elsewhere in this report. You should carefully read the "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section of this report titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a commercial-stage biopharmaceutical company with a mission to develop transformative therapies for people suffering from diseases with high unmet medical needs, with an initial focus on diseases of the central nervous system, or CNS. Our company was founded on the premise that the upper nasal space can be an optimal treatment entry point for CNS and other diseases where rapid vascular absorption can result in superior clinical outcomes. Our strategy is to pair our proprietary Precision Olfactory Delivery, or POD, upper nasal delivery technology with well-established therapeutics or other therapeutics where rapid vascular absorption is preferred to drive therapeutic benefit, improve patient outcomes, reduce drug development risk and expand the commercial opportunity within our target diseases. On September 2, 2021 Trudhesa was approved by the U.S. Food and Drug Administration, or FDA, for the acute treatment of migraine headaches with or without aura in adult patients.

We have retained all development and commercial rights to Trudhesa. Given the concentrated prescriber base of our target market for Trudhesa, we independently launched in October 2021. Trudhesa was launched with an initial sales force of 60 representatives and expanded to approximately 90 representatives in Q3 2022 to support our targeted launch strategy. The sales team is supported by an established market access, medical affairs, marketing, and operations infrastructure. Our commercial efforts are focused on approximately 11,000 high value HCP targets that prescribe approximately 40% of all migraine TRx and 73% of all acute branded total prescriptions. Importantly, we have secured managed care contracts providing access to Trudhesa for greater than 80% of commercial lives in the United States. We have deployed a robust sample program to ensure trial with Trudhesa for patients seeking better treatments and outcomes. Through both our commercial and medical affairs infrastructure we have engaged healthcare practitioners and patients, partnered with national associations and actively supported advocacy groups in the migraine market. These efforts have been, and will continue to be, supplemented with non-personal promotion to all targeted and non-targeted medium value physicians. To capture the maximum commercial opportunity of Trudhesa, we may also selectively seek partners to commercialize the product outside of our target markets, including additional penetration within the broader primary care setting, as well as in geographies outside of the United States. Through December 31, 2022, there have been approximately 62,600 prescriptions of Trudhesa generated since launch and, based on third-party data, we believe Trudhesa accounts for approximately 4.3% of total branded acute migraine prescriptions among over 2,400 unique Trudhesa prescribers since launch. Additionally, based on internal data, approximately 63% of new Trudhesa patients eligible for a refill have received a second prescription.

On February 22, 2023, we announced plans to reduce our workforce by approximately 16% and expect to incur a charge of approximately $1.5 million primarily consisting of severance costs, employee-related benefits, supplemental one-time termination payments, and asset write-downs in the first quarter of 2023. We plan to reprioritize spend to capitalize on the continued positive momentum in payor and prescriber uptake of Trudhesa and will halt research and development efforts on our prior product candidate INP105 to address acute agitation and aggression in autism spectrum disorder.

Prior to February 2023, we had built out an internal research and development team and also used third-party contract research organizations, or CROs, to carry out preclinical and clinical development. We rely on third-party contract manufacturing organizations, or CMOs, to manufacture and supply our clinical materials to be used during the development of any future product candidates. These CMOs are currently manufacturing commercial stage POD devices for Trudhesa, which we also used for our Phase 1 clinical trial, our registration lots and our STOP301 trial.

Through December 31, 2022, we have funded our operations primarily through proceeds from the sale of equity securities, including proceeds from the sale and issuance of common stock, proceeds pursuant to the Revenue Interest Financing Agreement, or our deferred royalty obligation, redeemable convertible preferred stock, warrants, debt and convertible notes. We have incurred significant operating losses to date. Our net losses were $106.3 million and $76.7 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $321.1 million and a cash balance of $60.7 million.

Recent Developments

Recovery of Drug Application Fee

In November 2020, we paid the FDA an application fee of $2.9 million for a new drug application related to Trudhesa. We had previously requested a small business waiver for the application fee, which was denied by the FDA. We requested that the FDA reconsider the waiver request and in October 2022, upon further review the FDA granted us the waiver request. As a result we received a refund of the full $2.9 million fee from the FDA in the fourth quarter of 2022.

Open Market Sales Agreement

In May 2022, we entered into a sales agreement with Cowen and Company, LLC, as a sales agent, pursuant to which we may offer and sell shares of our common stock, from time to time, up to an aggregate amount of gross sales proceeds of $ 50.0 million through an at-the-market ("ATM") Program ("2022 ATM Program"), under the 2022 Shelf Registration Statement. As of December 31, 2022, we sold 542,500 shares of common stock at a weighted-average price per share of $9.25 pursuant to the 2022 ATM Program and received proceeds of approximately $4.3 million, net of commissions and fees.

Oaktree Financing and Revenue Interest Financing

On March 17, 2022, we entered into a senior secured loan agreement and related security agreements or the Senior Credit Agreement with Oaktree Fund Administration, LLC as administrative agent, and the lenders party thereto, or collectively Oaktree, under which we borrowed $50.0 million less transactions costs (see Liquidity and Capital Resources - *Recent Debt Financings*).

Concurrently on March 17, 2022, we entered into a Revenue Interest Financing Agreement or RIF with certain purchasers party thereto, collectively the Purchasers, and Oaktree Fund Administration, LLC as administrative agent, pursuant to which we sold to the Purchasers the right to receive payments from us at a tiered percentage, or the Applicable Tiered Percentage, of future net revenues of Trudhesa, including worldwide net product sales and upfront payments, and milestones, together the Revenue Interests (see Liquidity and Capital Resources - Recent Debt Financings).

The inclusion of a going concern explanatory paragraph in the report of our independent registered public accounting firm on our accompanying financial statements for the fiscal year ended December 31, 2022 has resulted in a violation of certain covenants under Senior Credit Agreement with Oaktree. On March 22, 2023, we entered into a letter agreement (the “Oaktree Letter Agreement”) in connection with our Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from such going concern explanatory paragraph included in the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022.

Financial Operations Overview

Product Revenues, Net

We began to recognize revenue from product sales, net of discounts and other adjustments, in September of 2021 in conjunction with the launch of Trudhesa. We will continue to evaluate trends related to revenue momentum for Trudhesa. At launch we implemented our “bridge and co-pay savings” program which we believe provides an affordability solution for patients that enables higher physician prescribing. The program only provides assistance to commercially insured patients. Our data suggests these programs are playing an important role in supporting demand for Trudhesa.

Cost of Goods Sold

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of Trudhesa, including third-party manufacturing costs, packaging services, and freight-in.

Operating Expenses

Research and Development

Research and development costs are expensed as incurred. Research and development expenses consist primarily of salaries, benefits and other staff-related costs, including associated stock-based compensation, laboratory supplies, nonclinical and clinical studies and trials, manufacturing, costs for any future product candidates and POD devices to support our studies and trials, to design new versions of PODs, vendor validation and quality control preparation and fees paid to other entities that conduct certain research and development activities on our behalf. We consider regulatory approval of any future product candidates to be uncertain, and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. We expense manufacturing costs as incurred to research and development expense for any future product candidates prior to regulatory approval. If, and when, regulatory approval of a product is obtained, we begin to capitalize manufacturing costs related to the approved product into inventory.

We accrue for costs incurred as the services are being provided by monitoring the status of the trial or project and the invoices received from our external service providers. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed. In addition, we account for fully refundable research and development tax credits, based on 43.5% of qualified research and development expenditures of our Australian subsidiary, as an offset to research and development expenses.

Prior to our strategic reprioritization in February 2023, we tracked our direct costs by product candidate, but we do not allocate overhead costs or certain external costs because they support multiple future product candidates. In particular, with respect to internal costs, several of our departments support multiple future product candidate research and development programs, and we do not allocate those costs by product candidate.

Selling, General and Administrative

Our selling, general and administrative expenses consist primarily of employee-related expenses, including salaries, benefits, travel and stock-based compensation for our personnel in executive, finance and accounting, human resources, and other administrative functions, as well as fees paid for accounting, legal and tax services, consulting fees and facilities costs not otherwise included in research and development expenses. With the approval of Trudhesa in September 2021, we expect our selling and marketing costs will continue to remain significant as we continue to support our commercial activities associated Trudhesa. We incur additional expenses associated with operating as a public company, including increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with the rules and regulations of the SEC and standards applicable to companies listed on a national securities exchange, additional insurance expenses, investor relations activities and other administrative and professional services.

Other (Expense) Income, Net

Other (expense) income, net, consists of interest earned on our cash, interest expense on our borrowings, and changes in the fair value of our stock warrant liabilities, derivatives, redeemable convertible preferred stock warrant liabilities and convertible notes, and loss on extinguishment of debt.

Consolidated Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following tables summarize our results of operations for the periods presented.

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Product revenue, net	$ 12,652	$ 668	$ 11,984
Cost of goods sold	6,495	691	5,804
Gross profit (loss)	6,157	(23)	6,180
Operating expenses:			
Research and development	11,456	20,563	(9,107)
Selling, general and administrative	77,885	50,900	26,985
Total operating expenses	89,341	71,463	17,878
Loss from operations	(83,184)	(71,486)	(11,698)
Other (expense) income, net	(23,128)	(5,048)	(18,080)
Loss before income taxes	(106,312)	(76,534)	(29,778)
Provision for income taxes	-	2	(2)
Net loss and comprehensive loss	(106,312)	(76,536)	(29,776)
Accretion on redeemable convertible preferred stock	-	(129)	129
Net loss attributable to common stockholders	$ (106,312)	$ (76,665)	$ (29,647)

Product revenue, net

We recorded net product revenue in 2021 following FDA approval of Trudhesa in September 2021. We commenced shipments of Trudhesa during September 2021 and fully launched with a deployed sales force in October 2021. Net product revenue was $12.7 million for the year ended December 31, 2022, compared to $0.7 million for the year ended December 31, 2021. The increase of $12.0 million in net product revenues was due to both increased Trudhesa sales volumes as a result of full year of Trudhesa sales in 2022 and improvements in net price realization. Sales allowances and accruals recorded as an offset to product revenue mostly consisted of the bridge and co-pay savings program discounts, managed care rebates and distribution fees.

Cost of goods sold

Cost of goods sold of $6.5 million for the year ended December 31, 2022 compared to $0.7 million for the year ended December 31, 2021. The increase of $5.8 million was due to the increased product sales of Trudhesa in 2022 and reflects costs related to manufacturing, conversion and packing costs, in addition to certain overhead costs related to the cost of Trudhesa products sold. Inventory amounts written down to net realizable value as a result of obsolescence, scrap or other reasons charged to cost of goods sold totaled $0.1 million and $0.2 million for the year ended December 31, 2022 and 2021, respectively.

Prior to receiving FDA approval for Trudhesa in September 2021, we recorded all costs incurred in the manufacture of Trudhesa to be sold upon commercialization as research and development expense. As a result, a portion of the manufacturing costs related to the Trudhesa build-up incurred before FDA approval were already expensed in a prior period, referred to as zero cost inventories, and are therefore excluded from the cost of goods sold in the year ended December 31, 2022 and 2021. We sold all remaining zero cost inventories in 2022.

Research and Development

Research and development expenses were $11.5 million for the year ended December 31, 2022, compared to $20.6 million for the year ended December 31, 2021. The decrease of $9.1 million was primarily due to Trudhesa related costs, including personnel costs which were expensed as research and development rather than commercial costs prior to FDA approval in September 2021, and a refund under the small business waiver provision from the FDA in the amount of $2.9 million related to PDUFA fees paid in 2020 associated with the Trudhesa application. These costs were partially offset by an increase related to the clinical trial of our prior product candidate, INP105 in the year ended December 31, 2022 compared to the same period in 2021. As noted above, we halted research and development efforts on INP105 in February 2023.

The following table summarizes the period-over-period change in research and development expenses by historical product candidate for the periods indicated:

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Program-specific costs:			
Trudhesa	$ (454)	$ 7,785	$ (8,239)
INP105	3,202	2,728	474
Other programs	8	28	(20)
Total program-specific costs	2,756	10,541	(7,785)
Non program-specific costs:			
Personnel-related	$ 8,033	$ 9,686	$ (1,653)
Internal, overhead and other expenses	667	336	331
Total non program-specific costs	8,700	10,022	(1,322)
Total research and development expenses	$ 11,456	$ 20,563	$ (9,107)

Selling, General and Administrative

Selling, general and administrative expenses were $77.9 million in 2022, compared to $50.9 million in 2021. The increase of $27.0 million was primarily due to increases in spending to support commercial sales of Trudhesa. Commercial operations and sales related expenses increased $23.0 million to $40.0 million in 2022 compared to 2021 due to the timing and expansion of the sales force, partially offset by decreased marketing costs. Administrative expenses increased $3.3 million to $17.1 million in 2022 compared to 2021 primarily due to increased insurance, personnel, facilities and professional fees. Non-cash share-based compensation expense was $4.4 million for 2022, an increase of $1.9 million compared to the same period in 2021.

Other (Expense) Income, Net

Other (expense) income, net was an expense of $22.4 million for the year ended December 31, 2022, compared to expense of $5.0 million for the year ended December 31, 2021. The increase in expense of $17.3 million was primarily due to (i) an increase in the fair value of our RIF and Term Loan derivatives of $8.9 million related to changes in (a) the amount and timing of future royalty payments and (b) expectations of timing and probability of occurrence of a change in control and event of default, (ii) an increase in net interest expense of $8.3 million related to our borrowings under the RIF, Oaktree term loan and the Oxford and Silicon Valley Bank (SVB) Term Loan, and (iii) an increase of $1.3 million for the loss on early extinguishment. These increases were partially offset by a decrease in fair value adjustments of $1.2 million related to the 2021 convertible promissory notes and the common stock warrants.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses and negative cash flows from our operations. Through December 31, 2022, we have funded our operations primarily through the issuance of common stock, proceeds pursuant to the RIF, convertible promissory notes, redeemable convertible preferred stock, debt, and warrants with aggregate proceeds of $397.8 million. As of December 31, 2022, we had available cash and cash equivalents of $60.7 million and an accumulated deficit of $321.1 million.

We have an effective shelf registration statement on Form S-3 filed with the SEC in May 2022, or the 2022 Shelf Registration, pursuant to which we registered for sale up to $200 million of any combination of our common stock, preferred stock, debt securities, warrants, subscription rights and/or units from time to time and at prices and on terms that we may determine. In May 2022, we entered into a sales agreement with Cowen and Company, LLC, as a sales agent, pursuant to which we may offer and sell shares of our common stock, from time to time, up to an aggregate amount of gross sales proceeds of $50.0 million through an at-the-market program, or the 2022 ATM program under the 2022 Shelf Registration. In July 2022, we sold 542,500 shares of common stock at a weighted-average price per share of $9.25 pursuant to the 2022 ATM Program and received proceeds of approximately $4.5 million, net of commissions and fees.

Based upon our current operating plan, we estimate that our cash and cash equivalents as of December 31, 2022, are insufficient for us to fund operating, investing, and financing cash flow needs for twelve months subsequent to the issuance date of the financial statements included in this Annual Report on Form 10-K and accordingly, we have determined that there is substantial doubt about our ability to continue as a going concern.

Our loan agreement with Oaktree includes covenants requiring us to provide an audit opinion on our annual financial statements that is not subject to any “going concern” or like qualification or exception. On March 22, 2023, we entered into the Oaktree Letter Agreement in connection with our Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from the going concern explanatory paragraph included in the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022. The Senior Credit Agreement also requires us to maintain a minimum $12.5 million unrestricted cash balance at all times. We plan to address this condition through raising additional equity financings, or through other capital sources, including collaborations with other companies or other strategic transactions. To the extent that we may need to raise additional funds by issuing equity securities, our stockholders may experience significant dilution. If sufficient funds on acceptable terms are not available when needed, we could be required to reduce operating expenses and reduce the scope of our commercialization plans for Trudhesa. Failure to manage discretionary spending or raise additional financing, may adversely impact our ability to achieve our intended business objectives. Our consolidated financial statements as of and for the year ended December 31, 2022 do not include any adjustments that might result from the unfavorable outcome of this uncertainty.

Recent Debt Financings

Oaktree Facility

On March 17, 2022, or the Closing Date, we entered into a senior secured loan agreement and related security agreements or the Senior Credit Agreement with Oaktree Fund Administration, LLC as administrative agent, and the lenders party thereto, or collectively Oaktree, under which we borrowed $50.0 million. The term loan has a maturity date of March 17, 2027, initially bearing interest at the Secured Overnight Financing Rate, or SOFR, + 8.75% (with a SOFR floor of 1.00%). Once Trudhesa achieves at least $125.0 million in net sales, interest will step down to SOFR + 8.00% (with a SOFR floor of 1.00%).

We are required to make quarterly interest-only payments until the fourth anniversary of the Closing Date, after which we are required to make quarterly amortizing payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. Prepayments of the loan, in whole or in part, will subject to early prepayment fee which declines each year until the fourth anniversary date of the Closing Date, after which no prepayment fee is required. We are

also required to pay an exit fee upon any payment or prepayment equal to 2.0% of the aggregate principal amount of the loans funded under the Senior Credit Agreement. The Senior Credit Agreement contains customary representations, warranties and events of default. If we default under our Senior Credit Agreement, the lenders may accelerate all of our repayment obligations and take control of our pledged assets. The lenders could declare us in default under its debt obligation upon the occurrence of any event that the lenders interpret as having a material adverse effect as defined under the Senior Credit Agreement and the Revenue Interest Financing Agreement, thereby requiring us to repay the loans immediately or to attempt to reverse the lenders' declaration through negotiation or litigation. Among other loan covenant requirements, the Senior Credit Agreement also requires us to provide an audit opinion of our annual financial statements not subject to any "going concern" or like qualification or exception or explanatory paragraph of going concern footnote, however, any such audit report shall not be considered qualified due to the inclusion of an explanatory paragraph paragraph in the audit opinion based on the impending maturity date of any indebtedness within twelve months from the date of issuance of these financial statements, the prospective breach of any financial covenant hereunder or liquidity issues due to ordinary course liabilities. On March 22, 2023, we entered into the Oaktree Letter Agreement in connection with our Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from the going concern explanatory paragraph included in the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022. We are subject to a minimum liquidity requirement of $12.5 million unrestricted cash balance at all times.

A portion of the loan proceeds were used to repay in full the $32.9 million aggregate principal amount (including the prepayment fee and final payment fee) of loans outstanding owed to Oxford Finance LLC, or Oxford and Silicon Valley Bank, or SVB by the Company and as a result we recorded a $3.3 million loss on early extinguishment debt charge in 2022.

Revenue Interest Financing Agreement

On March 17, 2022 or the Effective Date, we entered into a Revenue Interest Financing Agreement, or RIF, with certain purchasers party thereto, collectively the Purchasers, and Oaktree Fund Administration, LLC as administrative agent, in such capacity, the RIF Agent, pursuant to which we sold to the Purchasers the right to receive payments from us at a tiered percentage, or the Applicable Tiered Percentage, of future net revenues of Trudhesa, including worldwide net product sales and upfront payments, and milestones, collectively, the Revenue Interests. Under the terms of the agreement, we received $50.0 million, the Investment Amount, less certain transaction expenses in exchange for tiered royalty payments on worldwide net sales from Trudhesa, as follows: 7.75% on annual United States net sales up to $150.0 million; 4.75% on annual United States net sales between $150 million and $300 million; 0.75% on annual United States net sales greater than $300.0 million; and 10% of any upfront payments, milestone payments and royalties received by us from licensing or partnerships relating to Trudhesa outside the United States.

The Purchaser's rights to receive the Revenue Interests shall terminate on the date on which the Purchasers have received payments equal to 175% of the funded portion of the Investment Amount including the aggregate of all payments made to the Purchasers as of such date, unless the RIF is earlier terminated. If the Purchasers have not received payments equal to the 175% of the funded portion of the Investment Amount by the nine-year anniversary of the initial closing date, among other things, we shall pay the Purchasers an amount equal to the funded portion of the Investment Amount plus a specific annual rate of return less payments previously received.

Under the RIF, we have an option, or the Call Option, to repurchase future Revenue Interests at any time until the third anniversary of the Closing Date upon advance written notice. Additionally, the Purchasers have an option, or the Put Option, to terminate the RIF and to require us to repurchase future Revenue Interests upon enumerated events such as a bankruptcy event, a material adverse effect including an event of default under the Senior Credit Agreement (such as a breach of the minimum liquidity covenant) or a change of control. If the Put Option or the Call Option are exercised, the required repurchase price is an amount equal to (i) as of any date before the one-year anniversary of the Effective Date, an amount equal to (a) 1.25 multiplied by (b) the Investment Amount, (ii) as of any date on or after the one-year anniversary of the Closing Date and before the two-year anniversary of the Closing Date, an amount equal to (a) 1.40 multiplied by (b) the

Investment Amount, (iii) as of any date on or after the two-year anniversary of the Closing Date and before the three-year anniversary of the Closing Date, an amount equal to (a) 1.55 multiplied by (b) the Investment Amount, and (iv) as of any date on or after the three-year anniversary of the Closing Date, an amount equal to (a) 1.75 multiplied by (b) the Investment Amount, in each case net of the sum of any payments received by the Purchasers prior to such Put Option Closing Date or Call Option Closing Date, as applicable.

If the Purchasers have not received 100% of the Investment Amount by February 15, 2027, the first tier royalty rate will be subject to an increase from 7.75% to 10.75%. The Company's obligations under the RIF are secured, subject to customary permitted liens and other agreed upon exceptions and subject to an intercreditor agreement with Oaktree Fund Administration, LLC, as administrative agent for the lenders under the Senior Credit Agreement, by a perfected security interest in (i) accounts receivable arising from net sales of Trudhesa and (ii) intellectual property that is claiming or covering Trudhesa, or any method of using, making or manufacturing Trudhesa, including regulatory approvals, clinical data and all other Trudhesa assets.

Cash Flows

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash provided by (used in):		
Cash used in operating activities	$ (93,642)	$ (66,364)
Cash used in investing activities	(1,377)	(408)
Cash provided by financing activities	67,461	147,889
Net increase (decrease) in cash	$ (27,558)	$ 81,117

Cash Flows From Operating Activities

For 2022, cash used in operating activities was $93.6 million, which consisted of a net loss of $106.3 million and an increase of $13.0 million in net current assets partially offset by $25.7 million in non-cash charges. The $13.0 million net cash outflow related to changes in our net current assets and was attributed to an increase in accounts receivables, inventories, operating leases and prepaid expenses and other current assets of $14.9 million offset by an increase in accrued liabilities of $1.9 million due primarily to an increase in the level of selling, general and administrative expenses. The non-cash charges primarily consisted of a change in the fair value of our derivative liabilities, stock-based compensation, depreciation and amortization, loss on early extinguishment of debt, amortization of debt discount, inventory write-downs to net realizable value, and a change in the fair value of our warrant liabilities.

For 2021, cash used in operating activities was $66.4 million, which consisted of a net loss of $76.5 million partially offset by a decrease of $2.2 million in net current assets and by $8.1 million in non-cash charges. The $2.2 million net cash inflow related to changes in our net current assets and was attributed to an increase in inventories, accounts receivables and prepaid expenses and other current assets of $5.5 million offset by an increase in accounts payable and accrued liabilities of $7.7 million due primarily to an increase in the level of selling, general and administrative expenses. The non-cash charges primarily consisted of stock-based compensation, depreciation and amortization, loss on early extinguishment of debt, amortization of debt discount, inventory write-downs to net realizable value, a change in the fair value of convertible notes, and a change in the fair value of our warrant liabilities.

Cash Flows From Investing Activities

For 2022 and 2021, cash used in investing activities of $1.4 million and $0.4 million, respectively, was related to purchases of property and equipment.

Cash Flows From Financing Activities

For 2022, cash provided by financing activities was $67.5 million, consisting primarily of net proceeds received from the Oaktree Financing and Revenue Interest Financing resulting in proceeds of $95.9 million, net of debt issuance costs and discount and proceeds of $4.3 million from the issuance of common stock under the 2022 ATM Program partially offset by the repayment of the Oxford and Silicon Valley Bank loan of $32.9 million including the final payment and prepayment fee.

For 2021, cash provided by financing activities was $147.9 million, consisting primarily of net proceeds received from our IPO of $72.0 million and follow-on offering of $48.3 million net of issuance costs, net proceeds of $19.1 million under the Loan Agreement, proceeds of $7.5 million from the issuance of convertible notes and to a lesser extent from exercises of stock options and exercise of redeemable convertible preferred stock warrants.

Funding Requirements

We use our cash to fund operating expenses, including research and development expenditures and commercialization expenses for Trudhesa. We incur significant commercialization expenses for product sales, marketing and outsourced manufacturing with respect to Trudhesa. On February 22, 2023, we announced plans to reduce our workforce by approximately 16%. These actions reflect our determination to reprioritize spend to capitalize on the continued positive momentum in payor and prescriber uptake of Trudhesa and as a result we will halt research and development efforts on INP105 to address acute agitation and aggression in autism spectrum disorder. We expect to record restructuring charges of approximately $1.5 million in the aggregate primarily consisting of severance costs, employee-related benefits, supplemental one-time termination payments, and asset write-downs in the first quarter of 2023.

Even in light of the reduction in workforce, we expect to continue to incur significant expenses and operating losses for the foreseeable future. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs primarily through equity financings.

The timing and amount of our operating expenditures will depend largely on:

- the costs and timing of commercialization activities, including product manufacturing, marketing, sales and distribution for Trudhesa, or any future product candidates for which we receive marketing approval;
- the number and development requirements of any future product candidates that we may pursue;
- the costs associated with building out our operations;
- the revenue, if any, received from commercial sales of any future product candidates for which we receive marketing approval;
- our ability to establish strategic collaborations;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the risk/benefit profile, cost and reimbursement policies with respect to any future product candidates, if approved, and existing and potential future therapies that compete with any future product candidates; and
- the costs associated with being a public company.

If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights.

Critical Accounting Policies, Significant Judgments and Use of Estimates

Our management's discussion and analysis of our financial condition and consolidated results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted

accounting principles, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported revenue generated, and reported expenses incurred during the reporting periods. Our estimates are based on our 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. Our actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in Note 2 "Summary of Significant Accounting Policies" in the notes to our financial statements, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements

Revenue Recognition

We recognize revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers (“ASC 606”). 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.

Product Revenue, Net

Subsequent to its regulatory approval in the U.S. in September 2021, the Company began to sell Trudhesa in the U.S. The product is distributed through an exclusive third-party logistics, or 3PL, distribution agent that does not take title to the product. The 3PL distributes Trudhesa to the customers, specialty pharmacies and specialty distributors (collectively referred to as "customers"), who then distribute the product to health care providers and patients. In our exclusive distribution agreement with the 3PL company, we act as principal because we retain control of the product.

Revenue from product sales is recognized when the customer obtains control of our product, which occurs upon transfer of title to the customer. We classify payments to customers or other parties in the distribution channel for services that are distinct and priced at fair value as selling, general and administrative expenses in our consolidated statements of operations. Payments to customers or other parties in the distribution channel that do not meet those criteria are classified as a reduction of revenue, as discussed further below. Taxes collected from the customer relating to product sales and remitted to governmental authorities are excluded from revenue. Because our payment terms are generally forty-five days, we conclude there is not a significant financing component because the period between the transfer of a promised good or service to the customer and when the customer pays for that good or service will be one year or less. We expense incremental costs of obtaining a contract as and when incurred since the expected amortization period of the asset that we would have recognized is one year or less.

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or the transaction price, which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, co-pay assistance, chargebacks, rebates and other allowances that are offered within contracts between us and our customer, health care providers and other indirect customers relating to the sale of Trudhesa. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or a current liability. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. 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.

The following are the components of variable consideration related to product revenue:

- Product Returns: Customers have limited return rights related to the product's damage or defect. We estimate the amount of product sales that may be returned and record the estimate as a reduction of revenue and a refund liability in the period the related product revenue is recognized. Based on the distribution model for Trudhesa and the price of Trudhesa, we believe there will be minimal returns.

- Other incentives: Other incentives include co-payment assistance we provide to patients with commercial insurance that have coverage and reside in states that allow co-payment assistance, as well as assistance in the form of a "bridge" program to help start a patient on a new therapy, especially in cases where payers may have barriers (e.g. prior authorizations and appeals) in place before agreeing to pay for a new drug. Under the bridge program the customer distributes the product free of cost to eligible individuals for a period of time. The volume of program utilization under the bridge and co-pay assistance programs is estimated by the Company at the time of sale to the customer. The calculation of the accrual for these programs is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue. The estimate is recorded as a reduction of revenue in the same period the related revenue is recognized.

- Managed care rebates: We are subject to rebates with certain commercial payers. We record these rebates as an accrual on our consolidated balance sheet in the same period we recognize the related revenue. We estimate our managed care rebates based on our estimated payer mix and the applicable contractual rebate rate.

- Chargebacks: We estimate obligations resulting from contractual commitments with the government and other entities to sell products to qualified healthcare providers and patients at prices lower than the list prices charged to our customers. The government and other entities charge us for the difference between what they pay for the product and the selling price to our customers. We record reserves for these chargebacks related to product sold to our customers during the reporting period, as well as our estimate of product that remains in the distribution channel at the end of the reporting period that we expect will be sold to qualified healthcare providers and patients in future periods. As of December 31, 2022, we did not enter into any contracts with entities that are eligible for chargebacks.

- Government rebates: We are subject to discount obligations under government programs, including Medicaid programs, Medicare and Tricare in the U.S. We estimate Medicaid, Medicare and Tricare rebates based upon a range of possible outcomes that are probability-weighted for the estimated payer mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a liability that is included in accrued expenses on our consolidated balance sheet. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. On a quarterly basis, we update our estimates and record any adjustments in the period that we identify the adjustments.

Accounts Receivable, net

Our trade accounts receivable consists of amounts due from customers in the U.S. net of distribution service fees, prompt pay discounts and other adjustments. Our contracts with customers have standard payment terms that generally require payment within 45 days. We analyze accounts that are past due for collectability, and periodically evaluate the creditworthiness of our customers. As of December 31, 2022, we determined an allowance for doubtful accounts was not required based upon our review of contractual payment terms and individual customer circumstances.

Inventory

Prior to receiving approval from the FDA in September 2021 to sell Trudhesa in the U.S., we expensed all costs incurred related to the manufacture of Trudhesa as research and development expense because of the inherent risks associated with the development of a drug candidate, the uncertainty about the regulatory approval process and the lack of history for our regulatory approval of drug candidates. Subsequent to receiving FDA approval in September 2021, we began

to capitalize inventory related costs that were incurred subsequent to FDA approval. we value our inventories at the lower-of-cost or net realizable value and determine the cost of our inventories, which includes costs related to products held for sale in the ordinary course of business, products in process of production for such sale and items to be currently consumed in the production of goods to be available for sale, on a first-in, first-out (FIFO) basis. Due to the nature of our supply chain process, inventory that is owned by us, is physically stored at third-party warehouses, logistics providers and contract manufacturers. Determining net realizable value of inventories involves significant judgments, including projecting future average selling prices and future sales volumes. To project average selling prices and sales volumes, we review recent sales volumes, prescription volumes, existing customer orders, general economic trends, and other information. When these analyses reflect estimated net realizable values below our manufacturing costs, we record a charge to cost of goods sold in advance of when inventories are actually sold. Differences in forecasted average selling prices used in calculating lower of cost or net realizable value adjustments can result in significant changes in the estimated net realizable value of product inventories and accordingly the amount of write-down recorded.

Stock-Based Compensation

We account for stock-based compensation expense related to stock options, restricted stock units, or RSUs, performance-based restricted stock units, or PSUs by estimating the fair value on the date of grant. The Company estimates the fair value of stock options granted to employees and non-employees using the Black-Scholes option pricing model. The fair value of RSUs and PSUs granted to employees is estimated based on the closing price of the Company's common stock on the date of grant.

Each PSU award reflects a target number of shares (“Target Shares”) that may be issued to the award recipient and the units earned at the end of the performance period will be determined based on the achievement of certain revenue targets over the performance period. The PSUs also include a performance objective relating to total shareholder return (“TSR”). TSR reflects the change in the value of the Company’s common stock over each performance period. Depending on the revenue achieved and the TSR during the two-year performance periods, the actual number of shares that a grant recipient receives at the end of the performance period may range from 0% to 125% of the Target Shares granted for the 2022 performance period and 0% to 150% of the Target Shares granted for the 2023 performance period.

Management assesses the probability of achieving the specified revenue targets at each reporting period based on current and expected performance of Trudhesa, In the period it becomes probable that the minimum threshold specified in the award will be achieved, we recognize expense for the proportionate share of the total fair value of the PSUs related to the vesting period that has already lapsed for the shares expected to vest and be released. The remaining fair value of the shares expected to vest and be released is expensed on a straight-line basis over the balance of the vesting period. In the event the Company determines it is no longer probable that we will achieve the minimum threshold specified in the award, we reverse all of the previously recognized compensation expense in the period such a determination is made.

The fair value of the portion of the Target Shares that relate to a relative TSR performance objective was determined using a Monte Carlo simulation analysis to estimate the total shareholder return ranking of the Company among a peer group over the remaining performance periods. See Note 9—Stock Incentive Plans to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further information.

Deferred Royalty Obligation

We account for the RIF, as discussed further in Note 6—Debt to our audited consolidated financial statements, as a deferred royalty obligation, amortized under the effective interest rate method over the estimated life of the revenue streams. We recognize interest expense thereon using the effective rate, which is based on our current estimates of future revenues over the life of the arrangement. In connection therewith, we periodically assess our expected revenues using internal projections, impute interest on the carrying value of the deferred royalty obligation, and record interest expense using the imputed effective interest rate. To the extent our estimates of future revenues are greater or less than previous

estimates or the estimated timing of such payments is materially different than previous estimates, we will account for any such changes by adjusting the effective interest rate on a prospective basis, with a corresponding impact to the reclassification of our deferred royalty obligation. The assumptions used in determining the expected repayment term of the deferred royalty obligation and amortization period of the issuance costs requires that we make estimates that could impact the short-term and long-term classification of such costs, as well as the period over which such costs will be amortized.

Derivative Liabilities

In connection with the borrowings under the RIF and the Senior Credit Agreement with Oaktree, we identified certain embedded derivatives, which are recorded as liabilities on the Company's consolidated balance sheet and are remeasured to fair value at each reporting date until the derivatives are settled. Changes in the fair value of the derivative liabilities are recognized as other income (expense) in the consolidated statement of operations and comprehensive loss. The fair value of the embedded derivative liabilities associated with the term loans was estimated using a probability weighted discounted cash flow model to measure the fair value. This involves significant Level 3 inputs and assumptions including an (i) estimated probability and timing of a change in control and events of default and ii) our risk-adjusted discount rate.

The embedded derivative liability associated with our deferred royalty obligation is measured at fair value using an option pricing Monte Carlo simulation model and is netted with the deferred royalty obligation in the consolidated financial statements. The assumptions used in the option pricing Monte Carlo simulation model include:(i) the probability-weighted net sales of Trudhesa; (ii) our risk-adjusted discount rate; (iii) our cost of debt; and (iv) the probability of a change in control and event of default occurring during the term of the instrument.

Recent Accounting Pronouncements

See Note 2—Basis of Presentation and Significant Accounting Policies to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information about recent accounting pronouncements, the timing of their adoption, and our assessment, to the extent we have made one yet, of their potential impact on our financial condition of results of operations.

JOBS Act Accounting Election

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 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 to enable us to get comply 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 emerging growth company 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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a smaller reporting company, we are not required to provide the information requested by this item pursuant to Item 305 of Regulation S-K.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Impel Pharmaceuticals Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Impel Pharmaceuticals Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss**,** changes in redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows for each of the two years in the period ended December 31, 2022, 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 at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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/ Ernst & Young LLP

We have served as the Company's auditor since 2017
Seattle, Washington
March 27, 2023

IMPEL PHARMACEUTICALS INC.
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 60,654	$ 88,212
Trade receivables, net	7,444	1,352
Inventory	8,427	2,824
Prepaid expenses and other current assets	3,284	2,188
Total current assets	79,809	94,576
Property and equipment, net	3,863	3,149
Operating lease right-of-use assets	3,132	—
Other assets	1,746	187
Total assets	$ 88,550	$ 97,912
Liabilities, and stockholders' (deficit) equity		
Current liabilities:		
Accounts payable	$ 6,092	$ 6,367
Accrued liabilities	12,242	8,950
Current portion of deferred royalty obligation	2,027	—
Current portion of operating lease liability	1,541	—
Common stock warrant liability	261	637
Total current liabilities	22,163	15,954
Operating lease liability, net of current portion	1,573	—
Deferred royalty obligation, net of current portion	60,899	—
Long-term debt	48,072	29,450
Total liabilities	132,707	45,404
Commitments and contingencies (Note 5)		
Stockholders' (deficit) equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; none issued	—	—
Common stock, $0.001 par value; 300,000,000 shares authorized; 23,739,313 and 23,123,062 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	24	23
Additional paid-in capital	276,929	267,283
Accumulated deficit	(321,110)	(214,798)
Total stockholders' (deficit) equity	(44,157)	52,508
Total liabilities, and stockholders' (deficit) equity	$ 88,550	$ 97,912

The accompanying notes are an integral part of these consolidated financial statements.

IMPEL PHARMACEUTICALS INC.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31,	
	2022	2021
Product revenue, net	$ 12,652	$ 668
Cost of goods sold	6,495	691
Gross profit (loss)	6,157	(23)
Operating expenses:		
Research and development	11,456	20,563
Selling, general and administrative	77,885	50,900
Total operating expenses	89,341	71,463
Loss from operations	(83,184)	(71,486)
Interest income (expense), net	(13,835)	(4,243)
Other income (expense), net	(9,293)	(805)
Loss before income taxes	(106,312)	(76,534)
Provision for income taxes	—	2
Net loss and comprehensive loss	$ (106,312)	$ (76,536)
Accretion on redeemable convertible preferred stock	—	(129)
Net loss attributable to common stockholders	$ (106,312)	$ (76,665)
Net loss per share attributable to common stockholders, basic and diluted	$ (4.53)	$ (5.25)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted	23,445,096	14,600,346

The accompanying notes are an integral part of these consolidated financial statements.

IMPEL PHARMACEUTICALS INC.
Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' (Deficit) Equity
(In thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount			
Balance —December 31, 2020	202,009,981	$ 127,039	755,478	$ —	$ 4,762	$ (138,262)	$ (133,500)
Accretion to redemption value on redeemable convertible preferred stock	—	129	—	—	(129)	—	(129)
Conversion of redeemable convertible preferred stock to common stock upon initial public offering	(202,009,981)	(127,168)	12,605,800	13	127,155	—	127,168
Proceeds from initial public offering, net of underwriters' discounts and commissions of $5.6 million and issuance costs of $2.4 million	—	—	5,333,334	5	71,992	—	71,997
Issuance of common stock upon exercise of warrants for cash	—	—	23,887	—	377	—	377
Issuance of common stock upon net exercise of warrants upon initial public offering		—	37,628	—	734	—	734
Issuance of common stock upon exchange of Avenue warrant	—	—	107,663	—	1,763	—	1,763
Conversion of convertible notes into common stock at initial public offering	—	—	559,585	1	8,392	—	8,393
Proceeds from follow-on public offering, net of underwriters' discounts and commissions of $2.8 million and issuance costs of $0.6 million	—	—	3,450,000	4	48,312	—	48,316
Stock-based compensation expense	—	—	—	—	3,130	—	3,130
Issuance of common stock upon the exercise of stock options	—	—	249,687	—	795	—	795
Net loss and comprehensive loss	—	—	—	—	—	(76,536)	(76,536)
Balance — December 31, 2021	—	$ —	23,123,062	$ 23	$ 267,283	$ (214,798)	$ 52,508
Stock-based compensation expense	—	—	—	—	5,191	—	5,191
Issuance of common stock upon the exercise of stock options	—	—	73,751	—	203	—	203
Issuance of common stock, net of issuance costs	—	—	542,500	1	4,252	—	4,253
Net loss and comprehensive loss	—	—	—	—	—	(106,312)	(106,312)
Balance — December 31, 2022	—	$ —	23,739,313	$ 24	$ 276,929	$ (321,110)	$ (44,157)

The accompanying notes are an integral part of these consolidated financial statements.

IMPEL PHARMACEUTICALS INC.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31, 2022	2021
Cash flows from operating activities:		
Net loss	$ (106,312)	$ (76,536)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,201	1,088
Non-cash lease expense	980	—
Stock-based compensation	5,191	3,130
Change in fair value of derivatives	9,655	—
Non-cash Interest on royalty obligation and other non cash interest	4,827	54
Loss on early extinguishment of debt	3,251	1,993
Change in fair value of convertible notes	—	839
Amortization of debt discount	810	714
Write-down of inventory to net realizable value	138	199
Change in fair value of warrant liabilities	(376)	(59)
Changes in operating assets and liabilities:		
Accounts receivable	(6,092)	(1,352)
Inventory	(5,753)	(3,023)
Prepaid expenses and other current assets	(1,095)	(1,111)
Accounts payable	(275)	1,999
Accrued liabilities	1,207	5,701
Operating Lease	(999)	—
Net cash used in operating activities	$ (93,642)	$ (66,364)
Cash flows from investing activities:		
Purchases of property and equipment	(1,377)	(408)
Net cash used in investing activities	$ (1,377)	$ (408)
Cash flows from financing activities:		
Proceeds from deferred royalty obligation, net of issuance costs	48,418	—
Proceeds from issuance of long-term debt, net of issuance costs	47,440	19,083
Payments on long-term debt, including final payment	(32,853)	—
Proceeds from issuance of common stock, net of issuance costs	4,253	120,313
Proceeds from issuance of convertible notes	—	7,500
Proceeds from exercise of redeemable convertible preferred stock warrants	—	197
Proceeds from issuance of common stock upon exercise of stock options	203	796
Net cash provided by financing activities	$ 67,461	$ 147,889
Net increase (decrease) in cash	(27,558)	81,117
Cash — Beginning of period	88,212	7,095
Cash — End of period	$ 60,654	$ 88,212
Supplemental disclosures of cash flow information:		
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 4,112	$ —
Recognition of embedded derivative	1,905	—
Accretion to redemption value on redeemable convertible preferred stock	—	129
Conversion of redeemable convertible preferred stock upon initial public offering	—	127,168
Issuance of common stock upon exchange / exercise of redeemable convertible preferred stock warrants upon initial public offering	—	2,677
Conversion of convertible notes into common stock upon initial public offering	—	8,393
Recognition of fair value of warrant liabilities issued in connection with issuance of debt	—	751
Purchase of property and equipment included in accounts payable and accrued liabilities	538	130
Accrued inventory purchases	1,547	—
Cash paid for interest	4,589	1,357

The accompanying notes are an integral part of these consolidated financial statements.

IMPEL PHARMACEUTICALS INC.
Notes to Consolidated Financial Statements

1. Organization and Description of Business

Impel Pharmaceuticals Inc. (“the Company”, "we", and "our"), is a commercial-stage biopharmaceutical company focused on the development and commercialization of transformative therapies for patients suffering from diseases with high unmet medical needs, with an initial focus on diseases of the central nervous system, or CNS. The Company's lead product, Trudhesa™ (dihydroergotamine mesylate) Nasal Spray was approved by the U.S. Food and Drug Administration ("FDA") on September 2, 2021. Using the Company’s proprietary Precision Olfactory Delivery (POD®) technology, Trudhesa™ gently delivers dihydroergotamine mesylate (DHE), a proven, well-established therapeutic, quickly to the bloodstream through the vascular-rich upper nasal space.

The Company’s strategy is to pair its POD®, upper nasal delivery technology with well-understood therapeutics or other therapeutics where rapid vascular absorption is preferred to drive therapeutic benefit, improve patient outcomes, reduce drug development risk and expand the commercial opportunity within its target diseases. The Company was incorporated under the laws of the State of Delaware on July 24, 2008, maintains its headquarters and principal operations in Seattle, Washington. In April 2022, the Company changed its name from Impel NeuroPharma, Inc. to Impel Pharmaceuticals Inc.

Initial Public Offering

On April 22, 2021, the Company’s Registration Statement on Form S-1 relating to its initial public offering, or IPO, was declared effective by the Securities and Exchange Commission, or the SEC, and the shares of its common stock began trading on the Nasdaq Global Select Market on April 23, 2021. The IPO closed on April 27, 2021, pursuant to which the Company issued and sold 5,333,334 shares of its common stock at a public offering price of $15.00 per share. The Company received net proceeds of approximately $72.0 million from the IPO, after deducting underwriting discounts and commissions of $5.6 million and offering costs of $2.4 million. Prior to the completion of the IPO, all shares of redeemable convertible preferred stock then outstanding were converted into 12,605,800 shares of common stock. In addition, the warrant held by Avenue Venture Opportunities Fund, L.P., or Avenue, was exchanged for 107,663 shares of common stock and warrants to purchase 1,987,348 shares of redeemable convertible preferred stock were cash exercised or automatically net exercised into an aggregate of 61,515 shares of common stock. The convertible notes issued in March 2021 for an aggregate principal amount of $7.5 million (see Note 6 - Debt) were also converted into 559,585 shares of common stock at a 10% discount of the IPO price.

Follow-on Public Offering

In September 2021, the Company completed a follow-on public offering of its common stock, pursuant to which the Company issued and sold 3,450,000 shares of its common stock (which included 450,000 shares that were offered and sold pursuant to the full exercise of the underwriters’ option to purchase additional shares) at a public offering price of $15.00 per share. Including the option exercise, the Company received net proceeds of approximately $48.3 million after deducting underwriting discounts and commissions of $2.8 million and offering costs of $0.6 million.

Reverse Stock Split

In April 2021, the Company’s board of directors and stockholders approved an amendment to the Company’s certificate of incorporation to effect a reverse split of shares of the Company’s common stock on an one-for-16.37332 basis, which was effected on April 16, 2021 (the “Reverse Stock Split”). The number of authorized shares and the par values of the common stock and redeemable convertible preferred stock were not adjusted as a result of the Reverse Stock Split. In connection with the Reverse Stock Split, the conversion ratio for the Company’s outstanding redeemable convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. All references to common stock and options to purchase common stock share data, per share data and related information contained in the consolidated financial statements have been retroactively adjusted to reflect the effect of the Reverse Stock Split for all periods presented.

Open Market Sales Agreement

In May 2022, the Company entered into a sales agreement with Cowen and Company, LLC, as a sales agent, pursuant to which the Company may offer and sell shares of its common stock, from time to time, up to an aggregate amount of gross sales proceeds of $50.0 million through an at-the-market ("ATM") Program ("2022 ATM Program"), under an effective shelf registration statement on Form S-3 ("2022 Shelf Registration Statement"). As of December 31, 2022, the Company sold 542,500 shares of common stock at a weighted-average price per share of $9.25 pursuant to the 2022 ATM Program and received proceeds of approximately $4.3 million, net of commissions and fees.

Liquidity and Capital Resources

From the Company's inception through December 31, 2022, it raised an aggregate of $397.7 million in proceeds from the issuance of its common stock, proceeds pursuant to the Revenue Interest Financing Agreement (deferred royalty obligation) ("RIF"), sale and issuance of redeemable convertible preferred stock, convertible notes, debt and warrants. The Company had a cash and cash equivalents balance of $60.7 million as of December 31, 2022. The Company currently has an effective 2022 Shelf Registration Statement on file with the Securities and Exchange Commission ("SEC"). The 2022 Shelf Registration Statement permits the offering, issuance and sale by the Company of up to an aggregate offering price of $200.0 million of common stock, preferred stock, debt securities, warrants, subscription rights and/or units in one or more offerings and in any combination.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. The Company had a cash and cash equivalents balance of $60.7 million as of December 31, 2022. Based upon the Company's current operating plan, it estimates that its cash and cash equivalents as of December 31, 2022 are insufficient for the Company to fund operating, investing, and financing cash flow needs for the twelve months subsequent to the issuance date of these financial statements. Accordingly, based on its recurring losses from operations, expected operating expenses going forward, and the need to raise additional capital to finance its future operations, the Company determined that there is substantial doubt about the Company's ability to continue as a going concern.

Further, the Senior Credit Agreement with Oaktree Fund Administration, LLC as administrative agent, and the lenders party thereto, or collectively Oaktree, as further described in Note 6, requires maintaining a minimum of $12.5 million in unrestricted cash and cash equivalents on hand to avoid an event of default under the Senior Credit Agreement. Based on our cash and cash equivalents on hand of approximately $60.7 million at December 31, 2022, the Company estimates that it will need to raise additional capital to avoid defaulting under its $12.5 million minimum cash liquidity covenant. Among other loan covenant requirements, the Senior Credit Agreement also requires the Company to provide an audit opinion of its annual financial statements not subject to any "going concern" or like qualification or exception or explanatory paragraph of going concern footnote, however, any such audit report shall not be considered qualified due to the inclusion of an explanatory paragraph paragraph in the audit opinion based on the impending maturity date of any indebtedness within twelve months from the date of issuance of these financial statements, the prospective breach of any financial covenant hereunder or liquidity issues due to ordinary course liabilities. If the Company defaults under its Senior Credit Agreement, the lenders may accelerate all of the Company's repayment obligations and take control of its pledged assets. The lenders could declare the Company in default under its debt obligation upon the occurrence of any event that the lenders interpret as having a material adverse effect as defined under the Senior Credit Agreement and the Revenue Interest Financing Agreement, thereby requiring the Company to repay the loans immediately or to attempt to reverse the lenders' declaration through negotiation or litigation. On March 22, 2023, the Company entered into the Oaktree Letter Agreement in connection with its Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from the going concern explanatory paragraph included in the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022.

The Company plans to address this condition through additional equity financings, or through other capital sources, including collaborations with other companies or other strategic transactions. To the extent that we may need to raise additional funds by issuing equity securities, our stockholders may experience significant dilution. If sufficient funds on acceptable terms are not available when needed, the Company could be required to reduce operating expenses and reduce the scope of its commercialization plans for Trudhesa. Failure to manage discretionary spending or raise additional financing, as needed, may adversely impact the Company's ability to achieve its intended business objectives. The accompanying financial statements do not reflect any adjustments relating to the recoverability and reclassifications of assets and liabilities that might be necessary if the Company is unable to continue as a going concern.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying audited consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The consolidated financial statements include the operations of Impel Pharmaceuticals Inc., and its wholly owned Australian subsidiary. All intercompany balances and transactions have been eliminated upon consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, management evaluates such estimates and assumptions for continued reasonableness. In particular, management makes estimates with respect to revenue recognition, inventory valuation, the fair values of derivative liabilities, stock-based compensation expense, deferred royalty obligation, lease accounting, and income taxes. Appropriate adjustments, if any, to the estimates used are made prospectively based upon such periodic evaluation. Actual results could differ from those estimates.

Segments

The Company's chief operating decision maker is its Chief Executive Officer. The Chief Executive Officer reviews financial information on an aggregate basis for the purposes of evaluating financial performance and allocating the Company's resources. Accordingly, the Company has determined that it operates in one segment. Substantially all of the Company's assets are located in the U.S.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents consist primarily of demand deposit accounts and deposits in short-term money market funds. At December 31, 2022 and December 31, 2021, cash consisted of cash in bank deposits held at financial institutions.

Accounts Receivable, net

The Company's trade accounts receivable consists of amounts due from specialty pharmacies and specialty distributors in the U.S. net of distribution service fees, prompt pay discounts and other adjustments. The Company's contracts with customers have standard payment terms that generally require payment within 45 days. The Company analyzes accounts that are past due for collectability, and periodically evaluates the creditworthiness of its customers. As of December 31, 2022 and 2021, we determined an allowance for doubtful accounts was not required based upon our review of contractual payment terms and individual customer circumstances.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") Topic 606, Revenue from Contracts with Customers ("ASC 606"). 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.

Product Revenue, Net

Subsequent to its regulatory approval in the U.S. in September 2021, the Company began to sell Trudhesa in the U.S. The product is distributed through an exclusive third-party logistics, or 3PL, distribution agent that does not take title to the product. The 3PL distributes Trudhesa to the Company's customers, specialty pharmacies and specialty distributor (collectively referred to as "customers"), who then distribute the product to health care providers and patients. In our exclusive distribution agreement with the 3PL company, the Company acts as principal because we retain control of the product.

Revenue from product sales is recognized when the customer obtains control of our product, which occurs upon transfer of title to the customer. We classify payments to customers or other parties in the distribution channel for services that are distinct and priced at fair value as selling, general and administrative expenses in our consolidated statements of operations. Payments to customers or other parties in the distribution channel that do not meet those criteria are classified as a reduction of revenue, as discussed further below. Taxes collected from the customer relating to product sales and remitted to governmental authorities are excluded from revenue. Because our payment terms are generally forty-five days,

we conclude there is not a significant financing component because the period between the transfer of a promised good or service to the customer and when the customer pays for that good or service will be one year or less. The Company expenses incremental costs of obtaining a contract as and when incurred since the expected amortization period of the asset that we would have recognized is one year or less.

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or the transaction price, which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, co-pay assistance, chargebacks, rebates and other allowances that are offered within contracts between us and our customer, health care providers and other indirect customers relating to the sale of Trudhesa. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or a current liability. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. 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.

The following are the components of variable consideration related to product revenue:

Product Returns: Customers have limited return rights related to the product's damage or defect. The Company estimates the amount of product sales that may be returned and records the estimate as a reduction of revenue and a refund liability in the period the related product revenue is recognized. Based on the distribution model for Trudhesa and the price of Trudhesa, the Company believes there will be minimal returns.

Other incentives: Other incentives include co-payment assistance the Company provides to patients with commercial insurance that have coverage and reside in states that allow co-payment assistance, as well as assistance in the form of a "bridge" program to help start a patient on a new therapy, especially in cases where payers may have barriers (e.g. prior authorizations and appeals) in place before agreeing to pay for a new drug. Under the bridge program the customer distributes the product free of cost to eligible individuals for a period of time. The volume of program utilization under the bridge and co-pay assistance programs is estimated by the Company at the time of sale to the Customer. The calculation of the accrual for these programs is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue. The estimate is recorded as a reduction of revenue in the same period the related revenue is recognized.

Managed care rebates: The Company is subject to rebates with certain commercial payers in the future. We record these rebates as an accrual on our consolidated balance sheet in the same period we recognize the related revenue. We estimate our managed care rebates based on our estimated payer mix and the applicable contractual rebate rate.

Chargebacks: The Company estimates obligations resulting from contractual commitments with the government and other entities to sell products to qualified healthcare providers and patients at prices lower than the list prices charged to our customers. The government and other entities charge us for the difference between what they pay for the product and the selling price to our customers. The Company records reserves for these chargebacks related to product sold to our customers during the reporting period, as well as our estimate of product that remains in the distribution channel at the end of the reporting period that we expect will be sold to qualified healthcare providers and patients in future periods. As of December 31, 2022, Impel did not enter into any contracts with government entities and other entities that are eligible for chargebacks.

Government rebates: The Company is subject to discount obligations under government programs, including Medicaid programs, Medicare and Tricare in the U.S. We estimate Medicaid, Medicare and Tricare rebates based upon a range of possible outcomes that are probability-weighted for the estimated payer mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a liability that is included in accrued expenses on our consolidated balance sheet. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. On a quarterly basis, we update our estimates and record any adjustments in the period that we identify the adjustments.

Inventory

Prior to receiving approval from the FDA in September 2021 to sell Trudhesa in the U.S., the Company expensed all costs incurred related to the manufacture of Trudhesa as research and development expense because of the inherent risks associated with the development of a drug candidate, the uncertainty about the regulatory approval process and the lack of history for the Company of regulatory approval of drug candidates. Subsequent to receiving FDA approval in September 2021, the Company began to capitalize inventory related costs that were incurred subsequent to FDA approval. The Company values its inventories at the lower-of-cost or net realizable value and determines the cost of its inventories, which includes costs related to products held for sale in the ordinary course of business, products in process of production for such sale and items to be currently consumed in the production of goods to be available for sale, on a first-in, first-out (FIFO) basis. Due to the nature of the Company's supply chain process, inventory that is owned by the Company, is physically stored at third-party warehouses, logistics providers and contract manufacturers. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess and obsolete inventories to their net realizable value in the period in which the impairment is first identified. If they occur, such impairment charges are recorded as a component of cost of goods sold in the consolidated statements of operations and comprehensive loss.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash. The Company's cash is deposited with high credit quality financial institutions. At times such deposits may be in excess of the Federal Depository Insurance Corporation insured limits.

The Company has exposure to credit risk in accounts receivable from sales of product. As of December 31, 2022, three customers accounted for 100% of the accounts receivable balance and revenues, with each of these individual customers ranging from 12% to 49% of the accounts receivable balance. As of December 31, 2021, two customers accounted for 100% of the accounts receivable balance and revenues, with each of these individual customers ranging from 46% to 54% of the accounts receivable balance.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the depreciable assets, ranging from three to four years. Property and equipment are primarily comprised of laboratory and platform equipment used to support manufacturing and research and development activities. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is reflected in the statement of operations in the year of disposition. Additions and improvements that increase the value or extend the life of an asset are capitalized. Repairs and maintenance costs are expensed as incurred. Leasehold improvements are amortized over the remaining term of the lease or the asset's useful life, whichever is shorter.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. The recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset or asset group to the estimated undiscounted future cash flows expected to be generated by the asset or asset group.

If the carrying amount of an asset or asset group exceeds its estimated undiscounted future cash flows, an impairment charge is recognized as the amount by which the carrying amount of the asset exceeds the estimated discounted future cash flows of the asset or asset group. There have been no such impairments of long-lived assets for any of the periods presented.

Fair Value Measurement

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use

of unobservable inputs. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active;

Level 3— Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the accompanying consolidated balance sheets for cash, other current assets, accounts payable, and accrued liabilities approximate their fair values, due to their short-term nature.

Leases

The Company adopted ASC Topic 842 - Leases, ("ASC 842") on January 1, 2022, effective January 1, 2022 using a modified retrospective method. The Company recognized $2.8 million of lease assets and liabilities and there was no impact to accumulated deficit upon adoption of ASC 842. The underlying assets of the Company's leases primarily relate to office space leases and a commercial vehicle fleet. The Company determines if an arrangement contains a lease at inception. The Company performed an evaluation of contracts in accordance with ASC 842 and has determined it has an operating lease agreement for the office facilities that the Company occupies and its commercial vehicle fleet. Operating lease right-of-use ("ROU") assets and operating lease liabilities are recognized at the date the underlying asset becomes available for the Company's use. Operating lease liabilities are based on the present value of the future minimum lease payments over the lease term. ROU assets are measured at the amount of the lease liability, adjusted for any initial direct costs incurred and any lease payments made at or before the lease commencement date, less lease incentives received. The Company uses the implicit rate when readily determinable and uses its incremental borrowing rate when the implicit rate is not readily determinable based upon the information available at the commencement date in determining the present value of the future minimum lease payments. The incremental borrowing rate is an estimate of the collateralized borrowing rate the Company would incur on its future lease payments over a similar term and is based on the information available to the Company at the lease commencement date, discussed in more detail below.

The Company's leases contain options to extend the leases; lease terms are adjusted for these options only when it is reasonably certain the Company will exercise these options. The Company's lease agreements do not contain residual value guarantees or covenants.

The Company has made a policy election regarding its real estate leases not to separate non-lease components from lease components, to the extent they are fixed. Non-lease components that are not fixed are expensed as incurred as variable lease expense. The Company's lease includes variable non-lease components, such as common-area maintenance costs. The Company has elected not to record on the balance sheet a lease that has a lease term of 12 months or less and does not contain a purchase option that the Company is reasonably certain to exercise. The Company accounts for leases with initial terms of 12 months or less as operating expenses on a straight-line basis over the lease term.

Lease expense is recognized within operating expenses on a straight-line basis over the terms of the lease. Incentives granted under the Company's facilities lease, including rent holidays, are recognized as adjustments to lease expense on a straight-line basis over the term of the lease.

Convertible Notes

In March 2021, the Company issued convertible promissory notes to various investors for an aggregate amount of $7.5 million. As permitted under Accounting Standards Codification ("ASC") 825, Financial Instruments ("ASC 825"), the Company elected the fair value option for recognition of the convertible notes. The Company elected the fair value option to allow the Company to eliminate the burden of complying with the requirements for derivative accounting. Under the fair

value option, the convertible notes were remeasured at fair value in each reporting period until their conversion in April 2021, with changes in the fair value recognized in the Company's consolidated statement of operations as other (expense) income, net. Accrued interest on the convertible notes is recorded in other (expense), net. The notes were automatically converted into shares of the Company's common stock upon the closing of the IPO in April 2021.

Cost of Goods Sold

Cost of goods sold consists primarily of third-party manufacturing, distribution, and overhead costs associated with Trudhesa. A portion of the costs of producing Trudhesa sold to date was expensed as research and development prior to the FDA approval of Trudhesa and, therefore, it is not reflected in the cost of goods sold.

Cost of goods sold for the year ended December 31, 2022 and 2021, included a charge of $0.1 and $0.2 million, respectively, to write down inventory to net realizable value in the consolidated statements of operations and comprehensive loss.

Research and Development Expense

Research and development costs are expensed as incurred and consist primarily of salaries, benefits and other staff-related costs, including associated stock-based compensation, laboratory supplies, nonclinical and clinical studies and trials and related clinical manufacturing costs, costs related to manufacturing preparation, fees paid to other entities that conduct certain research and development activities on the Company's behalf. Non-refundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses until the related goods are delivered or services are performed. Such payments are evaluated for current or long-term classification based on when such services are expected to be received.

The Company considers regulatory approval of product candidates to be uncertain, and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. The Company expenses manufacturing costs as incurred to research and development expense for product candidates prior to regulatory approval. If, and when, regulatory approval of a product is obtained, the Company begins capitalizing manufacturing costs related to the approved product into inventory.

Selling, General and Administrative Expense

Selling, general and administrative expenses are primarily comprised of compensation and benefits associated with sales and marketing, finance, human resources, legal, information technology and other administrative personnel, outside marketing, advertising and legal expenses and other general and administrative costs. The Company expenses the cost of advertising, including promotional expenses, as incurred. Advertising expenses were $7.6 million and $12.6 million for the years ended December 31, 2022 and 2021, respectively.

Advance Payments and Accruals for Research and Development Services

As part of the process of preparing its consolidated financial statements, the Company is required to estimate its expenses resulting from its obligation under contracts with vendors and consultants and clinical site agreements in connection with its research and development efforts. The financial terms of these contracts are subject to negotiations which vary contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts.

The Company's objective is to reflect the appropriate research and development expenses in its consolidated financial statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of its research and development efforts. The Company determines advance payments for research and development services and accrual estimates through discussion with applicable personnel and outside service providers as to the progress of clinical trials, or other services completed. The Company adjusts its rate of research and development expense recognition if actual results differ from its estimates. The Company makes estimates of its advance payments and accrued expenses as of each balance sheet date in its consolidated financial statements based on facts and circumstances known at that time. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low for any particular period. Through December 31, 2022, there had been no material adjustments to the Company's prior period estimates of advance payments and accruals for research and development expenses. The Company's

research and development advance payments and accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors.

Deferred Royalty Obligation

The Company accounts for the liability related to net revenues, as discussed further in Note 6, as a deferred royalty obligation, amortized under the effective interest rate method over the estimated life of the revenue streams. We recognize interest expense thereon using the effective rate, which is based on our current estimates of future revenues over the life of the arrangement. In connection therewith, we periodically assess our expected revenues using internal projections, impute interest on the carrying value of the deferred royalty obligation, and record interest expense using the imputed effective interest rate. To the extent our estimates of future revenues are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, we will account for any such changes by adjusting the effective interest rate on a prospective basis, with a corresponding impact to the reclassification of our deferred royalty obligation. The assumptions used in determining the expected repayment term of the deferred royalty obligation and amortization period of the issuance costs requires that we make estimates that could impact the short-term and long-term classification of such costs, as well as the period over which such costs will be amortized.

Derivative Liabilities

In connection with certain transactions, the Company has identified certain embedded derivatives, which are recorded as liabilities on the Company's consolidated Balance Sheet and are remeasured to fair value at each reporting date until the derivative is settled or expires. Changes in the fair value of the derivative liabilities are recognized as other income (expense) in the consolidated statement of operations and comprehensive loss. See Note 3 and 6 for additional details.

Warrant Liabilities

The Company determines the accounting classification of warrants that are issued, as either liability or equity, by first assessing whether the warrants meet liability classification in accordance with ASC 480-10, Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity, ("ASC 480-10"), and then in accordance with ASC 815-40, Derivatives and Hedging -- Contracts in Entity's Own Equity ("ASC 815-40"). Under ASC 480-10, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate the issuer to settle the warrants or the underlying shares by paying cash or other assets, or must or may require settlement by issuing variable number of shares.

If the warrants do not meet liability classification under ASC 480-10, the Company assesses the requirements under ASC 815-40, which states that contracts that require or may require the issuer to settle the contract for cash are liabilities recorded at fair value, irrespective of the likelihood of the transaction occurring that triggers the net cash settlement feature. If the warrants do not require liability classification under ASC 815-40, in order to conclude equity classification, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. After all relevant assessments are made, the Company concludes whether the warrants are classified as liability or equity. Liability classified warrants are required to be accounted for at fair value both on the date of issuance and on subsequent accounting period ending dates, with all changes in fair value after the issuance date recorded as a component of other income (expense), net in the accompanying consolidated statements of operations and comprehensive loss. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date. See Note 6 for additional details.

Stock-Based Compensation

The Company recognizes stock-based compensation expense for stock options and restricted stock unit awards on a straight-line basis over the requisite service period. The Company's stock-based compensation costs for stock options are based upon the grant date fair value of options estimated using the Black-Scholes-Merton option pricing model. This model utilizes as inputs the fair value of the underlying common stock at the measurement date, the estimated term of the stock options (weighted-average period of time that the options granted are expected to be outstanding), risk-free interest rates, expected dividends, and the expected volatility of the Company's common stock. The Company has elected to recognize forfeitures of share-based payment awards as they occur.

In determining the fair value of the stock options granted, the Company uses the Black-Scholes option-pricing model and assumptions discussed below.

Fair Value of Common Stock—Prior to the IPO, given the absence of a public trading market, the Company's board of directors with input from management considered numerous objective and subjective factors to determine the fair value

of common stock. The factors included, but were not limited to: (1) third-party valuations of the Company's common stock; (2) the Company's stage of development; (3) the status of research and development efforts; (4) the rights, preferences and privileges of the Company's preferred stock relative to those of the Company's common stock; (5) the Company's operating results and financial condition, including the Company's levels of available capital resources; and (6) equity market conditions affecting comparable public companies; (7) general U.S. market conditions; and (8) the lack of marketability of the Company's common stock. Following the IPO, as a public trading market for the Company's common stock has been established, the fair value of the common stock is determined based on the quoted market price of the common stock on the date of grant.

Expected Term—The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding. The Company used the simplified method (based on the mid-point between the vesting date and the end of the contractual term) to determine the expected term.

Expected Volatility—Since the Company recently completed its IPO and does not have substantial trading history for its common stock, the expected volatility was estimated based on the average historical volatilities for comparable publicly traded pharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle and area of specialty. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The Company recognizes stock-based compensation expense for stock options granted to non-employees based on the estimated fair value of the award as it is more readily measurable than the fair value of the services received.

Restricted stock units and performance stock units have a grant-date fair value equal to the fair market value of the underlying stock on the grant date. Compensation expense for performance stocks units with performance metrics is calculated based upon expected achievement of the metrics specified in the grant, or when a grant contains a market condition, the grant date fair value using a Monte Carlo simulation.

Income Taxes

Income taxes are accounted for using 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 or existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using the enacted tax 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 of enactment. The Company records a valuation allowance to reduce deferred tax assets to an amount for which realization is more likely than not.

The Company recognizes the tax benefit from an uncertain tax position if it is more likely than not that the tax position will be sustained upon examination by the tax authorities, based on the merits of the position. The Company does not believe any uncertain tax positions currently pending will have a material adverse effect on its consolidated financial statements nor does the Company expect any material change in its position in the next 12 months. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Net Loss Per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period, without consideration of potentially dilutive securities. Diluted net loss per share attributable to common stockholders is the same

as basic net loss per share attributable to common stockholders since the effect of potentially dilutive securities is anti-dilutive given the net loss of the Company.

Comprehensive Loss

Comprehensive loss represents the change in the Company's stockholders' equity (deficit) from all sources other than investments by or distributions to stockholders. The Company has no items of other comprehensive loss; as such, net loss equals comprehensive loss.

Recent Accounting Pronouncements Not Yet Adopted

Measurement of Credit Losses on Financial Instruments. In June 2016, the FASB issued guidance on the measurement of credit losses for financial assets measured at amortized cost, which includes accounts receivable. The new guidance replaces the existing incurred loss impairment model with an expected loss methodology, which will result in more timely recognition of credit losses. This update is effective for the Company for annual periods beginning after December 15, 2022, including interim periods within those annual periods. The adoption of this new guidance is not expected to have a material impact on our consolidated financial statements.

3. Fair Value Measurements

The following table summarizes the fair value of the Company's financial liabilities measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Common stock warrant liabilities	$ —	$ —	$ 261	$ 261
Derivative liability - Deferred royalty obligation	—	—	11,000	11,000
Derivative liability - Oaktree term loan	—	—	560	560
Total financial liabilities	$ —	$ —	$ 11,821	$ 11,821

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Common stock warrant liabilities	$ —	$ —	$ 637	$ 637
Total financial liabilities	$ —	$ —	$ 637	$ 637

The following table summarizes the change in the fair value of the common stock warrant liabilities (in thousands):

Balance as of December 31, 2020	$ —
Issuance of common stock warrants	751
Change in fair value	(114)
Balance as of December 31, 2021	$ 637
Change in fair value	(376)
Balance as of December 31, 2022	$ 261

The following table summarizes the change in the estimated fair value of the Company's derivative liabilities for the year ended December 31, 2022 (in thousands):

Beginning balance as of December 31, 2021	$ —
Initial fair value of derivative liability - Deferred royalty obligation	1,500
Initial fair value of derivative liability - Oaktree term loan	405
Changes in fair value of derivative liability - Deferred royalty obligation	9,500
Changes in fair value of derivative liability - Oaktree term loan	155
Ending balance as of December 31, 2022	$ 11,560

Fair values of the Company's common stock warrants and the derivative liabilities are based on significant inputs not observed in the market, and thus represent a Level 3 measurement.

The senior secured loan agreement and related security agreement with Oaktree Fund Administration, LLC, or the Oaktree Loan and Security Agreement, contains embedded derivatives requiring bifurcation as a derivative instrument. The derivative liability related to the Oaktree term loan is netted with the term loan in the consolidated financial statements see Note 6 for additional details. The fair value of the embedded derivative liabilities associated with the term loan was estimated using a probability weighted discounted cash flow model to measure the fair value. This involves significant Level 3 inputs and assumptions including an (i) estimated probability and timing of a change in control and event of default, and (ii) our risk-adjusted discount rate.

The embedded derivative liability associated with our deferred royalty obligation (see Note 6) is measured at fair value using an option pricing Monte Carlo simulation model and is netted with the deferred royalty obligation in the consolidated financial statements. The embedded derivative liability is subject to remeasurement at the end of each reporting period, with changes in fair value recognized as a component of other expense, net. The assumptions used in the option pricing Monte Carlo simulation model include:(i) the probability-weighted net sales of Trudhesa; (ii) our risk-adjusted discount rate; (iii) our cost of debt; and (iv) the probability of a change in control and event of default occurring during the term of the instrument. The effect of an increase or decrease of 5% of the probability of (i) a change in control, (ii) event of default and (iii) forecast net sales of Trudhesa, would result in a gain of $1.8 million or a loss of $1.7 million, respectively. The increase in the fair value of the embedded derivative liability at December 31, 2022 was based on changes in (a) the amount and timing of revenues and future royalty payments and (b) expectations of timing and probability of occurrence of a change in control and event of default.

Pursuant to the loan and security agreement with Oxford Finance LLC and Silicon Valley Bank, the Company issued common stock warrants (see Note 6). The Company's warrants are not indexed to the Company's common stock in the manner contemplated by ASC 815-40 because the warrant provides for an adjustment to the exercise price upon an acquisition. The Warrants were measured at fair value at inception and are subsequently remeasured at each reporting date with changes in fair value recognized as a component of other income (expense), net in the consolidated statement of operations and other comprehensive loss. The Company determined the fair value of the common stock warrants using the Black-Scholes-Merton option pricing model based on significant unobservable inputs. The significant unobservable inputs used in the fair value measurement of the warrant liabilities is the volatility rate which is based on the historical volatility of a set of peer companies, that are publicly traded.

4. Balance Sheet Components

Inventories

Inventories consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Raw materials	$ 2,461	$ 1,024
Work-in-process	4,191	876
Finished goods	3,334	924
Total inventories	9,986	—
Less: long-term inventories	(1,559)	—
Total current inventories	$ 8,427	$ 2,824

Inventory amounts written down to net realizable value in the consolidated statements of operations and comprehensive loss as a result of obsolescence, scrap or other reasons and charged to cost of goods sold totaled $0.1 million and $0.2 million during the year ended December 31, 2022 and 2021, respectively.

The Company classifies its inventories based on its anticipated levels of sales, any inventory in excess of its normal operating cycle is classified as long-term within Other Assets on its consolidated balance sheets.

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Other prepaids	$ 1,587	$ 793
Prepaid insurance	1,036	1,268
Other assets	649	105
Tax refund receivable	12	22
Total prepaid expenses and other current assets	$ 3,284	$ 2,188

Property and Equipment, Net

Property and Equipment, net consisted of the following (in thousands):

	December 31,	
	2022	2021
Laboratory and platform equipment	$ 6,990	$ 6,590
Furniture and office equipment	254	189
Leasehold improvements	199	198
Construction in progress	1,528	79
Total property and equipment, gross	8,971	7,056
Less: accumulated depreciation and amortization	(5,108)	(3,907)
Total property and equipment, net	$ 3,863	$ 3,149

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Accrued compensation	$ 5,287	$ 5,392
Accrued sales discounts and allowances	3,376	449
Accrued professional services	1,808	2,004
Accrued other liabilities	1,401	1,029
Accrued construction in progress	370	76
Total accrued liabilities	$ 12,242	$ 8,950

5. Commitments and Contingencies

Legal Proceedings

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. The Company has not recorded any such liabilities at either December 31, 2022 or 2021.

6. Debt

Oaktree Loan and Security Agreement

On March 17, 2022 (“Closing Date”), the Company entered into a senior secured loan agreement and related security agreements (“Senior Credit Agreement”) with Oaktree Fund Administration, LLC as administrative agent, and the lenders party thereto (collectively “Oaktree”) under which it borrowed $50.0 million.

The term loan has a maturity date of March 17, 2027, initially bearing interest at the Secured Overnight Financing Rate (“SOFR”) + 8.75 % (with a SOFR floor of 1.00%). Once Trudhesa achieves at least $125.0 million in net sales, interest will step down to SOFR + 8.00 % (with a SOFR floor of 1.00%). The Company is required to make quarterly interest-only payments until the fourth anniversary of the Closing Date, after which the Company is required to make quarterly amortizing

payments, with the remaining balance of the principal plus accrued and unpaid interest due at maturity. Prepayments of the loan, in whole or in part, will be subject to early prepayment fee which declines each year until the fourth anniversary date of the Closing Date, after which no prepayment fee is required. The Company is also required to pay an exit fee upon any prepayment equal to 2.0 % of the aggregate principal amount of the loans funded under the Senior Credit Agreement. The Senior Credit Agreement contains customary representations, warranties and events of default. If the Company defaults under its Senior Credit Agreement, the lenders may accelerate all of the Company's repayment obligations and take control of its pledged assets. The lenders could declare the Company in default under its debt obligation upon the occurrence of any event that the lenders interpret as having a material adverse effect as defined under the Senior Credit Agreement and the Revenue Interest Financing Agreement, thereby requiring the Company to repay the loans immediately or to attempt to reverse the lenders' declaration through negotiation or litigation. Among other loan covenant requirements, the Senior Credit Agreement also requires the Company to provide an audit opinion of its annual financial statements not subject to any "going concern" or like qualification or exception or explanatory paragraph of going concern footnote, however, any such audit report shall not be considered qualified due to the inclusion of an explanatory paragraph paragraph in the audit opinion based on the impending maturity date of any indebtedness within twelve months from the date of issuance of these financial statements, the prospective breach of any financial covenant hereunder or liquidity issues due to ordinary course liabilities. On March 22, 2023, the Company entered into the Oaktree Letter Agreement in connection with its Senior Credit Agreement, to obtain a waiver from Oaktree of any default or event of default arising from the going concern explanatory paragraph included in the report of its Independent Registered Public Accounting Firm on its audited consolidated financial statements for the year ended December 31, 2022. The Company is subject to a minimum liquidity requirement of $12.5 million unrestricted cash balance at all times.

The Company identified a number of embedded derivatives that require bifurcation from the term loan and that were separately accounted for in the consolidated financial statements as one compound derivative liability. Certain of these embedded features include change in control provisions, events of default and contingent rate increases. These embedded features met the criteria requiring these to be bifurcated because it was not clearly and closely related to the host instrument in accordance with ASC 815-15 and the derivative liability is presented separately as a long-term liability in the consolidated Balance Sheet as of December 31, 2022. The fair value of the embedded derivative liabilities associated with the term loans was estimated using the discounted cash flow method under the income approach. This involves significant Level 3 inputs and assumptions including an estimated probability and timing of a change in control and events of default (see Note 3 for additional details). The Company re-evaluates this assessment each reporting period. The initial recognition of the embedded derivative liability upon issuance of the Oaktree term loan was $0.4 million and at December 31, 2022 and is included in the term loan obligation in the consolidated Balance Sheet. At December 31, 2021 the fair value of the embedded derivative liability was $0.6 million.

In connection with the issuance of the term loan, the Company recorded debt discount and debt issuance costs of $2.9 million. The discount and issuance costs are amortized to interest expense using the effective interest method over the life of the term loan. The Company has elected to use the interest rate at inception of the term loan for purposes of the effective interest method. Interest expense for the year ended December 31, 2022 was $4.9 million, and is inclusive of non-cash amortization of the debt discount and debt issuance costs and accretion of final payment. The fair value of the term loan at December 31, 2022 was $51.9 million.

A portion of the loan proceeds were used to repay in full the $32.9 million aggregate principal amount (including the prepayment fee and final payment fee) of loans outstanding owed to Oxford and SVB by the Company.

Deferred Royalty Obligation

On March 17, 2022, the Company entered into a Revenue Interest Financing Agreement ("RIF" or "Deferred Royalty Obligation") with certain purchasers party thereto (collectively "Purchasers") and Oaktree Fund Administration, LLC as administrative agent, pursuant to which the Company sold to the Purchasers the right to receive payments from us at a tiered percentage (the "Applicable Tiered Percentage"), of future net revenues of Trudhesa, including worldwide net product sales and upfront payments, and milestones, (collectively, "the Revenue Interests"). Under the terms of the agreement, the Company received $50.0 million ("Investment Amount"), less transaction expenses, in exchange for tiered royalty payments on worldwide net sales from Trudhesa, as follows: 7.75% on annual United States net sales up to $150.0 million; 4.75% on annual United States net sales between $150 million and $300 million; 0.75% on annual United States net sales greater than $300.0 million; and 10% of any upfront payments, milestone payments and royalties received by us from licensing or partnerships relating to Trudhesa outside the United States.

The Purchaser's rights to receive the Revenue Interests shall terminate on the date on which the Purchasers have received payments equal to 175% of the funded portion of the Investment Amount including the aggregate of all payments made to the Purchasers as of such date, unless the Revenue Interest Financing Agreement is earlier terminated. If the

Purchasers have not received payments equal to the 175% of the funded portion of the Investment Amount by the nine-year anniversary of the initial closing date, among other things, the Company shall pay the Purchasers an amount equal to the funded portion of the Investment Amount plus a specific annual rate of return less payments previously received.

Under the RIF, the Company has an option (the "Call Option") to repurchase future Revenue Interests at any time until the third anniversary of the Closing Date upon advance written notice. Additionally, the Purchasers have an option (the "Put Option") to terminate the RIF and to require the Company to repurchase future Revenue Interests upon enumerated events such as a bankruptcy event, a material adverse effect including an event of default under the Senior Credit Agreement (such as a breach of the minimum liquidity covenant) or a change of control. If the Put Option or the Call Option are exercised, the required repurchase price is (i) as of any date before the one-year anniversary of the Closing Date, an amount equal to (a) 1.25 multiplied by (b) the Investment Amount, (ii) as of any date on or after the one-year anniversary of the Closing Date and before the two-year anniversary of the Closing Date, an amount equal to (a) 1.40 multiplied by (b) the Investment Amount, (iii) as of any date on or after the two-year anniversary of the Closing Date and before the three-year anniversary of the Closing Date, an amount equal to (a) 1.55 multiplied by (b) the Investment Amount, and (iv) as of any date on or after the three-year anniversary of the Closing Date, an amount equal to (a) 1.75 multiplied by (b) the Investment Amount, in each case net of the sum of any payments received by the Purchasers prior to such Put Option Closing Date or Call Option Closing Date, as applicable.

If the Purchasers have not received 100% of the Investment Amount by February 15, 2027, the first tier royalty rate will be subject to an increase from 7.75 % to 10.75%. The Company's obligations under the RIF are secured, subject to customary permitted liens and other agreed upon exceptions and subject to an intercreditor agreement with Oaktree Fund Administration, LLC, as administrative agent for the lenders under the Senior Credit Agreement, by a perfected security interest in (i) accounts receivable arising from net sales of Trudhesa and (ii) intellectual property that is claiming or covering Trudhesa, or any method of using, making or manufacturing Trudhesa, including regulatory approvals, clinical data and all other Trudhesa assets.

The Company evaluated the terms of the deferred royalty obligation and concluded that the features of the Investment Amount are similar to those of a debt instrument. Accordingly, the Company accounted for the transaction as long-term debt recorded at amortized cost using the effective interest method. The Company further evaluated the terms of the debt and determined that the Put Options under the RIF that are exercisable by Purchasers upon certain contingent events were determined to be embedded derivatives requiring bifurcation and separately accounted for as a single compound derivative instrument (see Note 3). The Put Option has been determined to qualify as an embedded derivative under ASC 815-40. The embedded derivative and the deferred royalty obligation have been netted to result in a net embedded derivative liability and is classified as a Level 3 financial liability in the fair value hierarchy as of December 31, 2022. The Company determined the fair value of the derivative using an option pricing Monte Carlo simulation model taking into account the probability of change of control or event of default occurring and potential repayment amounts and timing of such payments that would result under various scenarios, as further described in Note 3, "Fair Value of Financial Instruments". The Company recorded the initial fair value of the derivative liability of $1.5 million which is included in the deferred royalty obligation in the consolidated Balance Sheet. The Company remeasures the derivative liability to fair value each reporting period until the termination of the RIF. At December 31, 2022 the fair value of the derivative liability is $11.0 million.

The effective interest rate as of December 31, 2022 was 10.4%. In connection with the deferred royalty obligation, we incurred debt issuance costs totaling $1.4 million. Debt issuance costs have been netted against the debt as of December 31, 2022 and are being amortized over the estimated term of the debt using the effective interest method, adjusted on a prospective basis for changes in the underlying assumptions and inputs. The assumptions used in determining the expected repayment term of the obligation and amortization period of the issuance costs requires that we make estimates that could impact the short and long-term classification of these costs, as well as the period over which these costs will be amortized.

The Company periodically assesses the amount and timing of expected royalty payments using a combination of internal projections and forecasts from external sources. The estimates of future net product sales (and resulting royalty payments) are based on key assumptions including population, penetration, probability of success, and sales price, among others. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the deferred royalty obligations and the effective interest rate. Interest expense recognized for the year ended December 31, 2022 was

$5.5 million. The fair value of the deferred royalty obligation at December 31, 2022 is $48.9 million inclusive of the fair value of the derivative liability.

Oxford and Silicon Valley Bank Term Loan

On July 2, 2021, the Company entered into a loan and security agreement (the "Loan Agreement") with Oxford Finance LLC ("Oxford"), as the collateral agent and a lender, and Silicon Valley Bank ("SVB" and, together with Oxford, the "Lenders"), as a lender, pursuant to which the Lenders have agreed to lend the Company up to an aggregate of $50.0 million in a series of term loans (the "Term Loan"). Upon entering into the Loan Agreement, the Company received net proceeds of $9.2 million from the Lenders after deducting approximately $10.8 million of such amount applied to the repayment of the outstanding principal, interest and final payment fees owed pursuant to the Company's prior loan and security agreement with Avenue Venture Opportunities Fund, L.P. ("Avenue") dated November 5, 2020. On September 30, 2021, upon the achievement by the Company of NDA approval from the FDA of Trudhesa, the Company borrowed an additional $10.0 million.

The term loans accrued interest at the greater of (i) 7.95% or (ii) the sum of (a) the greater of (1) the thirty (30) day U.S. LIBOR or (2) 0.11%, plus (b) 7.84% and were subject to a prepayment fee of 1.0% to 3.0% depending upon when the prepayment occurs. On repayment of the Term Loans, the Company was required to make a final payment fee to the Lenders equal to 6.5% of the original principal amount of the Term Loans. Interest expense for the year ended December 31, 2022 was $0.7 million and was inclusive of non-cash amortization in the amount of $0.2 million related to the amortization of the debt issuance costs and accretion of final payment.

On March 17, 2022, upon entering into the Senior Credit Agreement, the Company paid the $30.0 million of outstanding principal, interest, including prepayment and final payment fees owed under the Loan Agreement to the Lenders. The Company evaluated whether the Senior Credit Agreement with Oaktree Fund Administration, LLC entered into in March 2022 represented a debt modification or extinguishment in accordance with ASC 470-50, Debt—Modifications and Extinguishments ("ASC 470-50") and determined that the existing Loan Agreement was extinguished as a result of the full repayment of the Term Loans and concurrent issuance of a new credit facility with new creditors, Oaktree. The Company recorded a loss of $3.3 million on the early extinguishment of debt related to the unamortized debt discount associated with the fair value of the warrants, final payment fee, and unamortized debt issuance costs. The loss on early extinguishment was recognized as a component of interest expense, net in the consolidated statement of operations and other comprehensive loss.

In connection with entering into the Loan Agreement and borrowings under the agreement, the Company issued warrants to purchase 71,522 and 23,166, shares of its common stock, respectively, to the Lenders at a per share exercisable price of $8.39 and $12.95, respectively, all with ten year terms.

Avenue Term Loan

On November 5, 2020 the Company entered into a debt and equity financing agreement with Avenue with $10.0 million ("Avenue Term Loan") funded at closing. In connection with the agreement, the Company granted Avenue warrants for the purchase of shares of 1,762,810 shares of Series D redeemable convertible preferred stock.

On July 2, 2021, upon entering into the Loan Agreement with Oxford and SVB, the $10.8 million of outstanding principal, interest and final payment fees owed under the debt and equity financing agreement with Avenue was repaid by the Lenders. The Company evaluated whether the Oxford and SVB credit facility entered into in July 2021 represented a debt modification or extinguishment in accordance with ASC 470-50 and determined that the existing Avenue Term Loan was extinguished as a result of the full repayment of the Avenue Term Loan and concurrent issuance of a new credit facility with new creditors, Oxford and SVB. The Company recorded a loss of $2.0 million on the early extinguishment of debt related to the unamortized debt discount associated with the fair value of the warrants, final payment fee, and unamortized debt issuance costs during the year ended December 31, 2021. The loss on early extinguishment was recognized as a component of other (expense) income, net in the consolidated statement of operations and other comprehensive loss.

Convertible Promissory Notes

In March 2021, the Company issued unsecured convertible promissory notes to various investors for an aggregate amount of $7.5 million which were accounted for at fair value. The notes bore interest at a rate of 5.0% per annum and mature on the earlier of (a) December 31, 2021 and (b) a change of control. The notes were automatically converted into shares of the Company's common stock upon the closing of the IPO in April 2021.

On March 31, 2021, the notes were remeasured to their settlement amount at the IPO date excluding accrued interest due to the proximity of the settlement date to the end of the reporting period. The loss on the increase in fair value on the convertible notes totaled $0.8 million from their issuance until settlement and is classified as other (expense) income, net in the accompanying consolidated statements of operations and comprehensive loss.

The carrying value of the convertible notes of $8.4 million immediately prior to the Company's IPO subsequently converted into 559,585 shares of common stock upon completion of the IPO.

7. Leases

The Company adopted ASC 842 using the modified retrospective approach, electing the practical expedient that allows us not to restate our comparative periods prior to the adoption of the standard on January 1, 2022. As such, the disclosures required under ASC 842 are not presented for periods before the date of adoption.

Real Estate Leases

In September 2017, the Company entered into a non-cancelable operating lease for 11,256 square feet of office and laboratory space. Rent is payable monthly, increasing by approximately 3% each year. The initial term of the lease was 3 years and the Company renewed the lease for an additional four years with an expiration date of August 31, 2024.

In December 2021 the Company entered into a non-cancelable operating lease for 7,051 square feet of office space with an expiration date of October 31, 2022. The Company occupied the temporary space for less than 12 months and did not record a right-of-use asset and lease liability on its balance sheet for the temporary space. The lease expired on October 31, 2022.

In April 2022 the Company entered into a non-cancelable operating lease for 8,045 square feet of office space. Rent is payable monthly, increasing by approximately 2.5 % each year. The term of the lease is 127 months, expecting to commence in the second quarter of 2023. Upon commencement, the Company will record a right-of-use asset and a lease liability on the consolidated Balance Sheet.

Commercial Fleet Leases

During 2022, the Company took delivery of a portion of its commercial car fleet for its salesforce. Each commercial fleet lease has a term of 12 months including options to renew for a total of 54 months, we believe a total of 36 months is deemed reasonable to exercise. In addition, the Company can terminate the vehicle leases at any time without a significant penalty. For the discount rate used in the commercial fleet lease, the Company used the weighted-average rate implicit in the commercial fleet leases.

As of December 31, 2022, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter are as follows (in thousands):

	Operating Leases
2023	1,662
2024	1,268
2025	354
Total undiscounted cash flows	3,284
Less: imputed interest	(170)
Total lease liabilities	3,114
Less: current portion	(1,541)
Lease liabilities	$ 1,573

The weighted average remaining lease term and the weighted average discount rate used to determine the operating lease liability were as follows:

	Operating Leases
Weighted average remaining lease term (years)	2.2
Weighted average discount rate	5.3%

Operating lease expense is $1.4 million for the year ended December 31, 2022. Variable lease expense is $0.4 million for operating leases during the year ended December 31, 2022. Rent expense recognized for short term leases was $0.2 million for the year ended December 31, 2022. Rent expense prior to the adoption of ASC 842 was $0.7 million for the year ended December 31, 2021.

8. Common Stock

Each share of common stock has the right to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the board of directors, subject to the prior rights of holders of all classes of stock outstanding having priority rights as to dividends. No cash dividends have been declared by the board of directors from inception.

The Company has reserved the following shares of common stock for issuance, on an as-converted basis, as follows:

	December 31, 2022	December 31, 2021
Stock incentive plans	6,113,763	5,324,202
Exercise of common stock warrants	94,688	94,688
Total	6,208,451	5,418,890

9. Stock Incentive Plans

2021 Equity Incentive Plan

The Company adopted its 2021 Stock Incentive Plan, or the 2021 Plan, and the Employee Stock Purchase Plan, or the ESPP, which became effective on the date immediately prior to the date of effectiveness of the IPO. The 2021 Plan serves as the successor to its 2018 Equity Incentive Plan (the "2018 Plan"). The 2021 Plan authorizes the award of stock options, RSUs, restricted stock awards, stock bonus awards, stock appreciation rights, performance awards, and cash awards. The number of Shares available for issuance under the 2021 Plan will increase automatically on January 1 of each of 2022 through 2031 by the lesser of (a) 5% of the total number of outstanding shares of all classes of its common stock on each December 31 and (b) a number as may be determined by its board of directors. The number of Shares available for issuance under the ESPP will increase automatically on January 1 of each of 2022 through 2031 by the lesser of (a) 1% of the total number of outstanding shares of all classes of its common stock on each December 31 and (b) a number as may be determined by its board of directors.

The Company initially reserved 2,205,000 shares of its common stock for the 2021 Plan, plus any reserved shares not issued or subject to outstanding grants under the 2018 Plan on the effective date of the 2021 Plan, for issuance pursuant to awards granted under its 2021 Plan. The total number of shares reserved for issuance under the 2021 Plan is 3,428,766 shares and approximately 1,330,624 shares were available for future grants as of December 31, 2022.

The Company initially reserved 276,000 shares of its common stock for the ESPP. The total number of shares reserved for issuance and available under the ESPP at December 31, 2022 is 507,230.

2008 Plan

In September 2008, the Company's board of directors adopted the 2008 Stock Incentive Plan, or the 2008 Plan, which provides for the granting of incentive stock options, nonqualified stock options, and restricted stock awards to its employees, directors and consultants. Options granted or shares issued under the 2008 Plan that were outstanding on the date the 2018 Equity Incentive Plan, or the 2018 Plan, became effective will remain subject to the terms of the 2008 Plan. The 2008 Plan terminated in 2018 as it reached its ten-year term. At December 31, 2022 and 2021, options to purchase 423,407 and 473,492 shares, respectively, under the 2008 Plan remained outstanding.

2018 Plan

In November 2018, the Company's board of directors adopted the 2018 Equity Incentive Plan. The 2018 Plan provides for the granting of incentive stock options, nonqualified stock options, restricted stock units, and other forms of stock awards to its employees, directors and consultants.

Under the 2018 Plan, the Company initially reserved 753,645 shares of common stock for issuance. In addition, any authorized shares not issued or subject to outstanding grants under the 2008 Plan and any shares subject to outstanding stock options that are cancelled without being exercised or expire under the 2008 Plan were added to the shares authorized and reserved for issuance under the 2018 Plan. In connection with the Board of Directors approval of the 2021 Plan, all remaining shares available for future award under the 2018 Plan were transferred to the 2021 Plan. At December 31, 2022 and 2021, options to purchase 1,849,875 and 1,892,106 shares, respectively, under 2018 Plan remained outstanding.

Effective January 1, 2022, the Company's 2021 Plan and ESPP reserves increased by 1,156,153 shares and 231,230 shares, respectively. Changes in shares available for grant under the 2021 Plan during the year ended December 31, 2022 were as follows:

	Shares Available for Grant
Shares available for grant at December 31, 2021	1,216,719
2021 Plan reserve increase January 1, 2022	1,156,153
ESPP reserve increase January 1, 2022	231,230
Options and restricted units granted	(1,251,345)
Options and restricted units forfeited, cancelled, or expired	485,097
Shares available for grant at December 31, 2022	1,837,854

Stock-Based Compensation Expense

Non-cash share-based compensation is measured at the grant date based on the fair value of the award and is recognized as expense over the requisite service period of the award using the straight-line method. Non-cash share-based compensation expense, consisting of expense for stock options, RSUs, and PSUs was classified in the consolidated statements of operations and comprehensive loss as follows (in thousands):

	Twelve Months Ended December 31,	
	2022	2021
Cost of goods sold	$ 58	$ 17
Research and development	768	657
General and administrative	4,365	2,456
Total stock-based compensation expense	$ 5,191	$ 3,130

The fair value of stock option awards granted to employees was estimated at the date of grant using a Black-Scholes-Merton option pricing model with the following assumptions:

	Twelve Months Ended December 31,	
	2022	2021
Expected term (in years)	6.1	6.1
Expected volatility	70.7% - 74.5%	59.2% - 85.5%
Risk-free interest rate	1.70% - 4.09%	0.42% - 1.30%
Expected dividends	—	—

Stock Option Activity

All stock option grants are awarded at fair value on the date of grant. The fair value of stock options is estimated using the Black-Scholes option pricing model and stock-based compensation is recognized on a straight-line basis over the requisite service period. Stock options granted generally become exercisable over a four-year period from the grant date. Stock options generally expire 10 years after the grant date.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common shares for those stock options that had exercise prices lower than the fair value of the Company's common shares at December 31, 2022.

A summary of the Company's stock option activity under its stock option plans was as follows (in thousands, except share and per share data and years):

	Number of Options	Weighted Average Exercise Price	Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Balance — December 31, 2021	3,345,912	$ 7.91	8.1	$ 6,662
Authorized	—			
Granted	1,251,345	9.12		
Exercised	(73,751)	2.76		
Cancelled	(247,597)	10.10		
Balance — December 31, 2022	4,275,909	$ 8.08	7.5	$ 1,038
Exercisable — December 31, 2022	2,276,891	$ 6.75	6.7	$ 1,019

As of December 31, 2022, there was $11.7 million of total unrecognized compensation cost related to unvested options that are expected to vest. The cost is expected to be recognized over a weighted-average period of 2.6 years.

The total fair value of options granted that vested during the years ended December 31, 2022 and 2021 was $0.5 million and $4.2 million, respectively.

The following table summarizes, at December 31, 2022, by price range: (1) for stock option awards outstanding under the stock incentive plans, the number of stock option awards outstanding, their weighted average remaining life and their weighted average exercise price; and (2) for stock option awards exercisable under the stock incentive plans, the number of stock option awards exercisable and their weighted average exercise price:

	Employees and Directors	
Exercise Price ($)	Shares Outstanding	Shares Exercisable
1.00 to 1.50	30,421	30,421
1.51 to 2.50	392,986	392,986
2.51 to 5.00	426,070	375,118
5.01 to 10.00	2,366,105	1,076,174
10.01 to 20.00	1,060,327	402,192
Total	4,275,909	2,276,891

Restricted Stock Units

The Company's Restricted Stock Units ("RSUs") are considered non-vested share awards and require no payment from the employee. For each RSU, employees receive one share of common stock at the end of the vesting period. The employee can elect to receive the one share of common stock net of taxes or pay for taxes separately and receive the entire share. The fair value of a restricted stock unit award at the grant date is equal to the market price of the Company's common stock on the grant date. Compensation expense is recorded based on the market price of the Company's common stock on the grant date and is recognized on a straight-line basis over the requisite service period. As of December 31, 2022 all granted RSUs had vested and there were no outstanding RSUs.

During 2021, the Compensation Committee of the Board of Directors approved the Trudhesa Launch Equity Incentive Plan for awards of performance-based restricted stock units (PSUs) to certain senior executives of the Company. Each award reflects a target number of shares ("Target Shares") that may be issued to the award recipient. These awards may be earned upon the completion of two-year performance periods ending December 31, 2022, and December 31, 2023. Whether units are earned at the end of the performance period will be determined based on the achievement of certain revenue targets over the performance period. The PSUs also include a performance objective relating to total shareholder return ("TSR"). TSR reflects the change in the value of the Company's common stock over each performance period. Depending on the revenue achieved and the TSR during the two-year performance periods, the actual number of shares

that a grant recipient receives at the end of the performance period may range from 0% to 125% of the Target Shares granted for the 2022 performance period and 0% to 150% of the Target Shares granted for the 2023 performance period.

In the period it becomes probable that the minimum threshold specified in the award will be achieved, we recognize expense for the proportionate share of the total fair value of the PSUs related to the vesting period that has already lapsed for the shares expected to vest and be released. The remaining fair value of the shares expected to vest and be released is expensed on a straight-line basis over the balance of the vesting period. In the event the Company determines it is no longer probable that we will achieve the minimum threshold specified in the award, we reverse all of the previously recognized compensation expense in the period such a determination is made.

The fair value of the Target Shares and restricted stock awards are based on the fair value of the underlying shares on the date of grant. The fair value of the portion of the Target Shares that relate to a relative TSR performance objective was determined using a Monte Carlo simulation analysis to estimate the total shareholder return ranking of the Company among a peer group over the remaining performance periods. The expected volatility of the Company's common stock at the date of grant was estimated based on the average historical volatilities for comparable publicly traded pharmaceutical companies. The Company used an expected dividend yield of zero. The risk-free interest rate assumption was based on observed interest rates consistent with the approximate two-year performance measurement period.

The fair value of PSUs granted to employees was estimated at the date of grant using the following assumptions:

	December 31, 2021
Contractual term (in years)	2.1
Expected volatility	0.83%
Risk-free interest rate	0.70%
Expected dividends	—

As of December 31, 2022, the Company does not expect these PSUs to vest, therefore there was no compensation expense recorded in 2022 and there is no unrecognized compensation expense remaining. There were no PSUs that vested during the year ended December 31, 2022.

The following table is a summary of the restricted stock unit activity for the year ended December 31, 2022:

	Number of RSUs	Weighted Average Grant Date Fair Value	Number of PSUs	Weighted Average Grant Date Fair Value
Unvested restricted stock outstanding as of December 31, 2021	10,571	$ 9.71	475,000	$ 9.33
Granted	—	—	—	—
Forfeited	—	—	(237,500)	—
Vested	(10,571)	9.71	—	—
Unvested restricted stock outstanding as of December 31, 2022	—	$ —	237,500	$ 9.33

10. Income Taxes

The components of loss before taxes were as follows (in thousands):

	Year Ended December 31, 2022	2021
Domestic	$ (106,279)	$ (76,512)
Foreign	(33)	(22)
Total loss before provision for income tax	$ (106,312)	$ (76,534)

The provision for income taxes consisted of the following (in thousands):

	Year Ended December 31,	
	2022	2021
Current:		
Federal	$ —	$ —
State	—	2
Foreign	—	—
Total current tax expense	$ —	$ 2

Reconciliation of income tax computed at federal statutory rates to the reported provision for income taxes was as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Tax provision at U.S. statutory rate	$ (22,325)	$ (16,072)
State taxes	(6,113)	(5,725)
Permanent differences	1,208	551
Embedded derivatives and warrants	1,949	-
Change in valuation allowance	26,043	21,567
Research and development credits	(503)	(576)
Other	(259)	257
Provision for income taxes	$ —	$ 2

Significant components of the Company's deferred income taxes at December 31, 2022 and 2021 are shown below (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating losses	$ 67,969	$ 44,540
Research and development and other tax credits	6,126	5,286
Capitalized research and development costs	2,473	—
Lease Liabilities	864	—
Other	2,565	2,964
Gross deferred tax assets	79,997	52,790
Less: Valuation allowance	(78,833)	(52,790)
Total deferred tax assets	1,164	—
Deferred tax Liabilities:		
Right of use asset	(869)	—
Other	(295)	—
Total deferred tax liabilities	(1,164)	—
Net deferred tax asset	$ —	$ —

The Tax Cuts and Jobs Act was enacted on December 22, 2017 and includes the requirement to capitalize and amortize research and experimental expenditures beginning in 2022. Prior to 2022, we expensed these costs as incurred for tax purposes. The capitalization of the research and experimental expenditures resulted in a new deferred tax asset of $2.4 million, which was offset by a valuation allowance, resulting in no significant impact to income tax expense for the year ended December 31, 2022. This deferred tax asset will be amortized over five and fifteen years depending on the whether the costs were incurred domestically or in foreign jurisdictions.

In accordance with the authoritative guidance for income taxes under ASC 740, a deferred tax asset or liability is recognized for the expected future tax consequences of temporary differences between the financial statement carrying amounts and tax bases of assets and liabilities.

At December 31, 2022 the Company had federal net operating loss, or NOL, and research and development credit carryforwards of approximately $21.4 million and $8.4 million, respectively. These carryforwards begin to expire in 2028 and 2029, respectively. In addition, the Company has $249.9 million of post 2017 federal NOL carryforwards that carry forward indefinitely. Utilization of the post 2017 federal NOL carryforwards is limited to eighty-percent of taxable income generated in a given tax year. The Company also has $153.4 million of state net operating losses, which begin to expire in 2035.

Under Sections 382 and 383 of the Internal Revenue Code of 1986 as amended, or IRC, the Company's NOL, and research and development credit carryforwards and other deferred tax assets may be limited or lost if cumulative changes in ownership exceeds 50% within any rolling three-year period. The Company has not completed an IRC Section 382/383 analysis regarding the limitation of NOL and credit carryforwards. If a change in ownership were to have occurred, the annual limitation may result in the expiration of NOL carryforwards and credits before utilization. If eliminated, the related asset would be removed from the deferred tax asset schedule with a corresponding reduction in the valuation allowance.

In evaluating its valuation allowance, the Company considers all available positive and negative evidence, including scheduled reversals of deferred tax liabilities, projected future taxable income, tax planning strategies, and recent financial performance. Due to uncertainty with respect to ultimate realizability of deferred tax assets, the Company has provided a valuation allowance against the U.S. deferred tax assets. The valuation allowance increased $26.0 million and $21.6 million in 2022 and 2021, respectively, primarily due to NOL's incurred during these periods.

The following table presents a reconciliation of the changes in the unrecognized tax benefit (in thousands):

Balance as of January 1, 2021		2,148
Decreases related to prior year tax positions		(117)
Increases related to current year tax positions		365
Balance as of December 31, 2021	$	2,396
Increases related to prior year tax positions		152
Increases related to current year tax positions		226
Balance as of December 31, 2022	$	2,774

The Company does not anticipate the amount of unrecognized tax benefits to significantly change within the next twelve months. Due to the valuation allowance recorded against the Company's deferred tax assets, none of the total unrecognized tax benefits as of December 31, 2022 and 2021 would reduce the effective tax rate if recognized. As of December 31, 2022 and 2021, there are no penalties recorded in the financial statements. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit.

The Company files tax returns with the U.S. and various state and Australian tax authorities. The Company currently has no years under examinations by any jurisdiction; however, the Company is subject to income tax examinations by Federal, California and Australian tax authorities for years beginning in 2019, 2018, and 2017, respectively. Further, to the extent allowed by law, the taxing authorities may have the right to examine prior originating periods when NOLs and tax credits are being utilized in the current year.

The Company has made the accounting policy election to recognize the impact of Global Intangible Low-Tax Income as a period cost.

11. Defined Contribution Plan

The Company has a defined contribution retirement savings plan under Section 401(k) of the IRC. This plan allows eligible employees to defer a portion of their annual compensation on a pre-tax or after-tax basis. The Company makes discretionary matching contributions of up to 4% of a participating employee's salary. For the year ended December 31, 2022 and 2021, the amount expensed under the plan was $0.8 million and $0.4 million, respectively.

12. Net Loss Per Share Attributable to Common Stockholders

The following outstanding shares of potentially dilutive securities were excluded from the computation of the diluted net loss per share attributable to common stockholders for the periods presented because their effect would have been anti-dilutive:

	Year Ended December 31,	
	2022	2021
Stock options to purchase common stock	4,275,909	3,345,912
Non-vested RSUs and PSUs	237,500	485,571
Warrants to purchase common stock	94,688	94,688
Total	4,608,097	3,926,171

13. Subsequent Events

On February 22, 2023, the Company announced plans to reduce its workforce by approximately 16% and expects to incur a charge of approximately $1.5 million primarily consisting of severance costs, employee-related benefits, supplemental one-time termination payments, and asset write-downs in the first quarter of 2023. The Company plans to reprioritize spend to capitalize on the continued positive momentum in payor and prescriber uptake of Trudhesa and will halt research and development efforts on INP105 to address acute agitation and aggression in autism spectrum disorder.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Under the supervision of and with the participation of our management, including our chief executive officer, who is our principal executive officer, and our chief financial officer, who is our principal financial officer, we conducted an evaluation of the effectiveness of our disclosure controls and procedures as of December 31, 2022, the end of the period covered by this Annual Report. The term "disclosure controls and procedures," as set forth in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our chief executive officer and chief financial officer and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Our management, with the participation of our chief executive officer and chief financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its *Internal Control – Integrated Framework (2013)*. Based on our assessment, our management has concluded that, as of December 31, 2022, our internal control over financial reporting is effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. For as long as we remain an "emerging growth company" as defined in Section 2(a) of the Securities Act of 1933, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fourth quarter of 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

On March 22, 2023, our Board of Directors approved the amended and restated bylaws (the "Amended and Restated Bylaws"), which became effective the same day. The amendments effected by the Amended and Restated Bylaws (i) revise certain provisions relating to adjournment procedures and lists of stockholders entitled to vote at stockholder meetings, in each case to conform to recent amendments to the DGCL, (ii) address matters relating to the SEC's adoption of the universal proxy rules in Rule 14a-19 of the Exchange Act, and (iii) clarify the adjournment procedures for virtual meetings of stockholders to reflect recent amendments to the DGCL. The foregoing description is not complete and is qualified in its entirety by reference to the full text of the Amended and Restated Bylaws, a copy of which is attached as Exhibit 3.2 hereto and is hereby incorporated by reference.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Except as set forth below, the information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Our independent public accounting firm is Ernst & Young LLP, Seattle, Washington, PCAOB Auditor ID 42.

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

Item 15. EXHIBITS, FINANCIAL SATEMENT SCHEDULES.

(1) All financial statements;

See Index to Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

All financial statement schedules have been omitted because the required information was not applicable or was not present in amounts sufficient to require submission of the schedules, or because the information required is included in the financial statements or the accompanying notes.

(3) Exhibits

The exhibits listed in the following Index to Exhibits are filed, furnished or incorporated by reference as part of this Annual Report on Form 10-K.

EXHIBIT INDEX

		Incorporated by Reference				
Exhibit No	Description of Exhibit	Form	File No.	Exhibit	Filing Date	Filed Herewith
3.1	Restated Certificate of Incorporation	10-Q	001-40353	3.1	June 7, 2021	
3.2	Amended and Restated Bylaws					X
4.1	Form of Registrant's Common Stock Certificate	S-1/A	333-254999	4.1	April 19, 2021	
4.2	Amended and Restated Investors' Rights Agreement, dated December 4, 2018, by and among the registrant and certain of its stockholders.	S-1	333-254999	4.2	April 2, 2021	
4.3	Form of 2021 Convertible Promissory Note.	S-1	333-254999	4.3	April 2, 2021	
4.4	Warrant to Purchase Common Stock issued by the Company on July 2, 2021, in favor of Silicon Valley Bank, pursuant to the Security and Loan Agreement, dated as of July 2, 2021, by and between the Registrant and Oxford Finance LLC and Silicon Valley Bank.	10-Q	001-40353	4.3	August 16, 2021	
4.5	Warrant to Purchase Common Stock issued by the Company on July 2, 2021, in favor of Oxford Finance, LLC pursuant to the Security and Loan Agreement, dated as of July 2, 2021, by and between the Registrant and Oxford Finance LLC and Silicon Valley Bank.	10-Q	001-40353	4.4	August 16, 2021	
4.6	Warrant to Purchase Common Stock issued by the Company on September 30, 2021, in favor of Oxford Finance, LLC pursuant to the Security and Loan Agreement, dated as of July 2, 2021, by and between the Registrant and Oxford Finance LLC and Silicon Valley Bank.	10-Q	001-40353	4.3	November 15, 2021	
4.7	Warrant to Purchase Common Stock issued by the Company on September 30, 2021, in favor of Silicon Valley Bank, pursuant to the Security and Loan Agreement, dated as of July 2, 2021, by and between the Registrant and Oxford Finance LLC and Silicon Valley Bank.	10-Q	001-40353	4.4	November 15, 2021	
10.1	Form of Indemnity Agreement.	S-1/A	333-254999	10.1	April 19, 2021	
10.2+	2008 Equity Incentive Plan, and forms of award agreements.	S-1	333-254999	10.2	April 2, 2021	
10.3+	2018 Equity Incentive Plan, and forms of award agreements.	S-1	333-254999	10.3	April 2, 2021	
10.4+	2021 Equity Incentive Plan, and forms of award agreements.	S-1/A	333-254999	10.4	April 19, 2021	
10.5+	2021 Employee Stock Purchase Plan, and forms of award agreements.	S-1/A	333-254999	10.5	April 19, 2021	
10.6+	Employment Agreement, dated April 15, 2021, by and between the registrant and Adrian Adams.	S-1/A	333-254999	10.6	April 19, 2021	
10.7+	Employment Agreement, dated April 15, 2021, by and between the registrant and Stephen Shrewsbury.	S-1/A	333-254999	10.7	April 19, 2021	
10.8+	Employment Agreement, dated April 15, 2021, by and between the registrant and John Leaman.	S-1/A	333-254999	10.8	April 19, 2021	
10.9+	Employment Agreement, dated April 15, 2021, by and between the registrant and Leonard Paolillo.	10-K	001-40353	10.9	March 29, 2022	
10.10	BMR-201 Elliott Avenue LLC Lease, dated July 19, 2017, by and between the registrant and BMR-201 Elliott Avenue LLC.	S-1	333-254999	10.9	April 2, 2021	
10.11	Security and Loan Agreement, dated as of July 2, 2021, by and between the Registrant and Oxford Finance LLC and Silicon Valley Bank.	10-Q	001-40353	10.4	August 16, 2021	

10.12	Credit Agreement and Guaranty dated as of March 17, 2022, by and among Impel Neuropharma, Inc., the subsidiary guarantors from time to time party thereto, the lenders from time to time party thereto, and Oaktree Fund Administration, LLC, as administrative agent.	10-Q	001-40353	10.1	May 16, 2022	
10.13	Revenue Interest Financing Agreement dated as of March 17, 2022, between Impel Neuropharma, Inc., the purchasers from time to time party thereto, and Oaktree Fund Administration, LLC, as administrative agent.	10-Q	001-40353	10.2	May 16, 2022	
10.14	Sales Agreement, dated May 16, 2022, by and between the Registrant and Cowen and Company LLC	S-3	333-264987	1.2	May 16, 2022	
10.15	Oaktree Letter Agreement dated as of March 22, 2023, between the Registrant and Oaktree Fund Administration, LLC, as administrative agent.					X
21.1	Subsidiaries of the Registrant.					X
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm.					X
24.1	Powers of Attorney. Reference is made to the signature page hereto.					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
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.					X
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.					X
101.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)					X

+ Indicates management contract or compensatory plan.

* The certification furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-Kand are deemed “filed” by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act of 1933 or the Exchange Act.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Impel Pharmaceuticals Inc.

Date: March 27, 2023

By: /s/ Adrian Adams

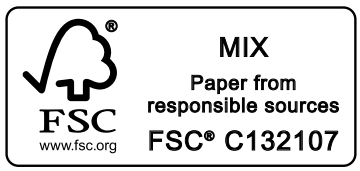
Adrian Adams
President and Chief Executive Officer
(Principal Executive Officer)

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Adrian Adams and Rajiv Amin, and each one of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in their name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K and to file the same, with Exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

/s/ Adrian Adams Adrian Adams	Chief Executive Officer and Director *(Principal Executive Officer)*	March 27, 2023
/s/ Rajiv Amin Rajiv Amin	Interim Chief Financial Officer *(Principal Accounting and Financial Officer)*	March 27, 2023
/s/ David Allison David Allison	Director	March 27, 2023
/s/ Tim Nelson Tim Nelson	Director	March 27, 2023
/s/ Ali Satvat Ali Satvat	Director	March 27, 2023
/s/ Diane Wilfong Diane Wilfong	Director	March 27, 2023
/s/ Stewart Parker Stewart Parker	Director	March 27, 2023
/s/ Mahendra Shah Mahendra Shah	Director	March 27, 2023

[THIS PAGE INTENTIONALLY LEFT BLANK]


FSC
www.fsc.org
MIX
Paper from
responsible sources
FSC® C132107