Risk Factors Comparison 2025-03-11 to 2024-03-28 Form: 10-K

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An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled " Risk Factors " prior to making an investment in our common stock. These risks include, but are not limited to, the following: • **Substantial doubt exists as to our ability to continue as a going concern. Our ability to continue as a going concern is subject to material uncertainty and dependent on our success at raising additional capital sufficient to meet our obligations on a timely basis.** If we fail to obtain additional financing when needed, we may be unable to complete the development, regulatory approval and commercialization of our product ~~candidates~~ **candidate** . • We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be materially adversely affected if we are unable to service our debt obligations. • Cytisinicline is currently our sole product candidate and there is no guarantee that we will be able to successfully develop and commercialize cytisinicline. • ~~We are~~ **The development and commercialization of our product candidate is** dependent upon **securing sufficient quantities of cytisinicline from trees and other plants, which grow outside of the United States in** a ~~single company~~ **limited number of locations. • We currently exclusively rely on Sopharma AD,** ~~for~~ **or** ~~the~~ **Sopharma, to** manufacture ~~and~~ **cytisinicline for use in clinical trials. We plan to engage other third parties for our manufacturing processes, including to manufacture future** supply of cytisinicline **on a commercial scale, if approved. Our commercialization of cytisinicline could be stopped, delayed or made less profitable if Sopharma fails to obtain approval of government regulators, fails to provide us with sufficient quantities of product or fails to do so at acceptable quality levels or prices** . • We plan to submit ~~an~~ **a** New Drug Application, or NDA, to the **U. S. Food and Drug Administration, or** FDA **,** for **the marketing** approval of cytisinicline as ~~an aid~~ **a drug therapy** in treating nicotine dependence for smoking cessation, based largely on data from our ~~recently~~ completed Phase 3 ORCA- 2 and ORCA- 3 clinical trials and ~~planned~~ **the ongoing** ORCA- OL trial; however, there can be no assurance that the data from our clinical trials will ultimately support an NDA filing or that the FDA will grant marketing approval of cytisinicline without additional clinical or nonclinical studies, or at all. • ~~The development of our product candidate is dependent upon securing sufficient quantities of cytisinicline from trees and other plants, which grow outside of the United States in a limited number of locations. •~~ If we do not obtain the necessary regulatory approvals in the United States and / or other countries, we will not be able to sell cytisinicline. • Cytisinicline may cause undesirable side effects or have other properties that could delay or prevent regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any. • It is difficult to evaluate our current business, predict our ~~future~~ prospects and forecast our financial performance and growth ~~. • We currently exclusively rely on Sopharma to manufacture cytisinicline for use in clinical trials and plan to engage other third parties for our manufacturing process, including to manufacture cytisinicline on a commercial scale, if approved. Our commercialization of cytisinicline could be stopped, delayed or made less profitable if Sopharma fails to obtain approval of government regulators, fails to provide us with sufficient quantities of product or fails to do so at acceptable quality levels or prices~~ . • We face substantial competition, and our competitors may discover, develop or commercialize products faster or more successfully than us ~~. • We may not be successful in obtaining or maintaining necessary rights to cytisinicline, product compounds and processes for our development pipeline through acquisitions and in- licenses~~ . ITEM 1. BUSINESS OVERVIEW OF OUR BUSINESS AND RECENT DEVELOPMENTS We are a ~~clinical~~ **late** - stage **clinical specialty** pharmaceutical company ~~committed~~ **with a sole mission** to **address** the global **nicotine dependence epidemic in combustible cigarette and e- cigarette usage through the** development and commercialization of cytisinicline ~~for smoking cessation~~ **. There are** ~~and~~ **an estimated 29** ~~nicotine addiction. With more than one billion people who use tobacco globally and over 28~~ million adults ~~who smoke~~ in the United States alone ~~, smoking remains~~ **who smoke combustible cigarettes and an estimated 11 million adults in the United States who utilize e- cigarettes. Tobacco use is currently** the leading cause of preventable ~~disease and~~ death ~~,~~ **and is** responsible for more than eight million deaths **worldwide and nearly half a million deaths in the United States** annually ~~worldwide~~ . ~~Our primary focus~~ **More than 87 % of lung cancer deaths, 61 % of all pulmonary disease deaths, and 32 % of all deaths from coronary heart disease are attributable to smoking and exposure to secondhand smoke. While nicotine e- cigarettes are thought to be less harmful than combustible cigarettes, they remain highly addictive and can deliver harmful chemicals which can cause lung injury or cardiovascular disease. In 2024, 1. 6 million high school and middle school students reported using e- cigarettes. Research shows adolescents who have used e- cigarettes are seven times more likely to become smokers one year later compared to those who have never used e- cigarettes. Recently, the U. S. Food and Drug Administration, or FDA, granted Breakthrough Therapy Designation for cytisinicline for nicotine e- cigarette, or vaping, cessation. Breakthrough Therapy Designation** is **a process that expedites the development and review of new drugs and biologics that are intended** to ~~address this global epidemic~~ **treat serious or life- threatening conditions and have preliminary clinical evidence indicating substantial improvement over existing therapies. Currently, there are no FDA approved drug therapies indicated specifically as an aid to nicotine e- cigarette cessation** . We believe ~~that~~ cytisinicline represents a unique opportunity to significantly impact global health by addressing the considerable unmet need among millions of smokers and e- cigarettes users. **We expect to file a New Drug Application, or NDA, with the FDA for treatment of nicotine dependence for smoking cessation at the end of the second quarter of 2025.** If approved ~~by the U. S. Food and Drug Administration~~ , **cytisinicline will** ~~or FDA, it stands to~~ become the first new prescription medicine in nearly two decades **for smoking cessation** ~~aimed at aiding individuals in overcoming nicotine~~

~~dependence~~. We believe cytisinicline is differentiated from existing smoking cessation treatments given ~~it~~ **its combination of efficacy, well- tolerated safety profile, and a shorter therapy duration,** ~~has~~ **as** demonstrated in **clinical trials. Dependent on availability of funding, we intend** ~~two~~ **to initiate** ~~randomized placebo controlled~~ Phase 3 **clinical development** ~~studies a combination~~ of **cytisinicline for** ~~robust efficacy, minimal frequency of side effects and optional shorter course of therapy. We plan to continue expanding our focus to address other methods of~~ nicotine **dependence for** ~~addiction such as~~ e- cigarettes / vaping ~~. The use of e- cigarettes continues to be widespread, with most recent reports from the Centers for Disease Control and Prevention indicating more than 11 million adult users~~ in ~~the United States alone in 2021. While e- cigarettes have been historically viewed as less harmful than combustible cigarettes, their long- term safety remains controversial. We believe that cytisinicline, if approved, could be~~ the first **half of 2026, which we expect** ~~prescription drug indicated for vape and e- cigarette users who are ready~~ to ~~quit~~ **complete approximately 12 months after initiation, and may explore additional indications for their** ~~--~~ **the treatment of** nicotine **dependence** ~~addiction. Our management team has significant experience~~ in ~~growing emerging companies focused on~~ the **future** ~~development of under- utilized pharmaceutical compounds to meet unmet medical needs. We intend to use this experience to develop and ultimately commercialize cytisinicline either directly or via strategic collaborations~~. Cytisinicline as our Product Candidate Our product candidate, cytisinicline, is a naturally occurring, plant- based alkaloid. In 2018, the U. S. Adopted Names Council adopted cytisinicline as the non- proprietary, or generic, name for the substance also known as cytisine. Cytisinicline is structurally similar to nicotine and has a well- defined, dual- acting mechanism of action ~~that is~~ **, being** both **a receptor** ~~agonistic~~ ~~--~~ **agonist** and ~~antagonistic~~ ~~--~~ **antagonist**. It is believed to ~~aid~~ **work** in **treating nicotine dependence for** smoking **and e- cigarette** cessation ~~and the treatment of nicotine addiction~~ by interacting with nicotine receptors in the brain by reducing the severity of ~~nicotine~~ withdrawal symptoms **,** ~~through agonistic effects on nicotine receptors~~ and ~~by~~ reducing the reward and satisfaction associated with nicotine ~~through antagonistic properties~~ **products. Cytisinicline is an investigational product candidate being developed for treatment of nicotine dependence and has not been approved by the FDA for any indication in the United States**. Cytisinicline as a 25- day downward titration regimen is an established smoking cessation treatment that has been approved and marketed in Central and Eastern Europe by Sopharma AD, or Sopharma, for over 20 years. It is estimated that over 20 million people have used Sopharma' s cytisinicline product to help treat nicotine ~~addiction~~ **dependence**. We have developed an improved dosage **, formulation,** and **simpler treatment schedule. The** administration of **our** cytisinicline ~~that~~ has demonstrated robust efficacy with minimal levels of adverse events in two randomized placebo **-** controlled Phase 3 studies. We have an exclusive license and **a** supply agreement with Sopharma for the development and commercialization of cytisinicline outside of Sopharma' s territories **,** which are predominately located in Central and Eastern Europe. Cytisinicline Mechanism of Action Cytisinicline ~~is a partial agonist that~~ binds with high affinity to the alpha- 4 beta- 2, or α4β2, nicotinic acetylcholine receptors in the brain. ~~Through dual- acting partial agonist / partial antagonist activity, cytisinicline is believed to help reduce nicotine cravings, withdrawal symptoms and reward and satisfaction associated with smoking.~~ The α4β2 nicotinic receptor is a well- understood target in ~~addiction~~ **dependence**. When nicotine binds to this receptor, it causes dopamine to be released in the mid- brain, reinforcing the dopamine reward system. This receptor has been implicated in the development and maintenance of nicotine ~~addiction~~ **dependence**. Cytisinicline is believed to act as a partial agonist ~~at the~~ **/ antagonist binding to** α4β2 nicotinic ~~receptor~~ **receptors** ~~, preventing~~ **in the brain and is thought to have two potential consequences in treating** nicotine ~~from~~ **dependence. First, the partial agonism maintains some release of dopamine (albeit at a very reduced level than that stimulated by nicotine) and therefore reduces nicotine craving, and second, the partial antagonism prevents nicotine** binding ~~and releasing dopamine~~ **so that nicotine no longer induces the same pleasure or reward stimulation**. Cytisinicline Opportunity We have an exclusive license and supply agreement with Sopharma for the development and commercialization of cytisinicline outside of Sopharma' s territory, which consists of certain countries in Central and Eastern Europe, Scandinavia, North Africa, the Middle East and Central Asia, as well as Vietnam. We ~~intend to develop and commercialize cytisinicline in the United States, and thereafter to target other markets outside of Sopharma' s territory, such as Western Europe, Japan, China, Australasia, Southeast Asia and Latin and South America. We~~ are developing cytisinicline as ~~an aid to~~ **a drug therapy in treating nicotine dependence for** smoking cessation and ~~treatment for nicotine addiction to~~ **e- cigarette cessation which would** address the limitations of both prescription drugs and of Over- the- Counter, or OTC, products. We believe that a substantial market exists in the United States, European Union, or EU, and the rest of the world for a **new,** safe and effective smoking cessation treatment. We believe cytisinicline is differentiated from existing smoking cessation treatments given its combination of robust efficacy, minimal frequency of side effects and optional shorter course of therapy, as shown in two randomized placebo **-** controlled Phase 3 studies. Our goal is to obtain approval from the FDA and from other regulatory agencies for the sale and distribution of cytisinicline in the United States and subsequently to other countries outside of Sopharma' s territory. OVERVIEW OF OUR REGULATORY PROGRESS AND CLINICAL PHASE 3 PROGRAM Overview of Regulatory Progress Smoking Cessation Indication In June 2017, we filed an Investigational New Drug Application, or IND, with the FDA, for evaluation of cytisinicline as a treatment for smoking cessation. This IND included required non- clinical toxicology studies that were sponsored by the National Center for Complementary and Integrative Health, or NCCIH, a division of the NIH and by the National Cancer Institute, or NCI, to assist in our IND for investigating cytisinicline as a smoking cessation treatment. In May 2018, we held an end of Phase 2 meeting with the FDA to review and receive guidance on our Phase 3 clinical program and overall development plans to support an NDA for the 25- day downward titration cytisinicline regimen. The FDA recommended to consider evaluating higher dosing, a more simplified daily regimen, and possible longer dosing in our development program. This FDA review also included our plans and their recommendations for non- clinical studies, standard drug- to- drug interaction and reproductive / teratogenicity studies. Detailed plans for chronic toxicology, carcinogenicity studies, and additional clinical studies regarding a maximum tolerated dose, renal impairment, QT interval prolongation, longer term exposure and adequate demonstration of safety and efficacy from planned randomized, placebo- controlled, Phase 3 clinical trials were also discussed. In December 2018, we announced that the

FDA agreed with our Initial Pediatric Study Plan, specifically, providing a full waiver for evaluating cytisinicline in a pediatric population. The reasons for the full waiver were based on the low numbers of children smoking under the age of 12 and the logistical difficulties of recruiting treatment- seeking smokers in the adolescent age group. The agreed upon Initial Pediatric Study Plan is expected to be included as part of our future application for marketing approval of cytisinicline. In November 2019, we held a type C meeting with the FDA to review results from our ~~recently conducted~~ Phase 2 ORCA- 1 study and our revisions to the Phase 3 clinical program using a simplified 3 mg **tablet administered three times a day, or** TID **,** dosing schedule. The FDA agreed that the 3 mg TID dosing schedule was acceptable for our Phase 3 clinical program. In March 2019, we had also initiated our Phase 1 clinical study to assess for dose limiting adverse effects, or AEs, that would define the maximum tolerated dose, or MTD, for a single administered oral dose of cytisinicline. Because dose limiting AEs for the MTD could not **be** reached **per protocol definitions** in the study, the results were reviewed with the FDA at this November 2019 Type C meeting, with an agreement that further escalation beyond the single 30 mg dose was not required in the study. Additional NCCIH and NCI sponsored non- clinical toxicology studies that evaluated reproductive toxicology and company sponsored non- clinical toxicology studies that evaluated longer cytisinicline ~~treatment~~ **exposure** beyond one month to at least three months for support in initiating our Phase 3 clinical program were submitted in 2020. This allowed the initiation of our two Phase 3 clinical trials in the fourth quarter of 2020 and first quarter of 2022. Additional plans for our Phase 1 studies regarding pharmacokinetics, or PK, assessments for subjects with renal impairment and evaluations for possible QT interval prolongation, which were first discussed with the FDA as part of the end of Phase 2 meeting in 2018, were followed by more detailed review and agreement with the FDA during 2022 and 2023. ~~Both~~ **These** studies have now been completed. During 2022 and 2023, we had several Type C and Type D meetings with the FDA regarding the adequacy of our completed nonclinical studies, overall clinical pharmacology information, manufacturing product information, and our Integrated Safety Summary, or ISS, analysis plans for a future NDA submission. In the fourth quarter of 2023, we initiated our pre- NDA discussions with the FDA regarding the adequacy of our efficacy and safety information for proceeding with an NDA submission. The FDA expressed support for an NDA submission based on adequate data to assess for efficacy from our two completed randomized and controlled Phase 3 trials. In addition, the FDA advised that long- term exposure data to assess for safety beyond 12 weeks would be needed to adequately assess safety risks given that the FDA views smoking cessation drugs as products for chronic, repeated, and intermittent use as patients may relapse and require subsequent courses of treatment over a lifetime. In the first quarter of 2024, we reached agreement with the FDA that a single, open- label study evaluating the long- term safety effects of cytisinicline will be sufficient to complete the requirement and enable an NDA submission anticipated ~~in~~ **at** the ~~first half~~ **end of the second quarter** of 2025. E- cigarette (vaping) Cessation Indication In July 2021, we announced that we were awarded a grant from the National Institute on Drug Abuse, or NIDA, of the National Institutes of Health, or NIH, to evaluate the use of cytisinicline as a treatment for cessation of nicotine e- cigarette use. This initial grant award was utilized to complete critical regulatory activities for the submission of a second IND to the FDA for evaluation of cytisinicline as a treatment for nicotine e- cigarette cessation, or vaping cessation. In November 2021, we announced that the FDA had completed their review and accepted this IND to investigate cytisinicline in this population. **In** ~~Based on~~ the ~~significant benefit~~ **third quarter of 2024, we received Breakthrough Therapy Designation** from **the FDA for** cytisinicline ~~treatment~~ **for nicotine e- cigarette,** ~~for~~ **or** vaping **,** cessation ~~shown in our completed Phase 2 trial~~ **. Breakthrough Therapy Designation is designed to expedite the development and review of drugs that are intended to treat serious conditions when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. It provides product sponsors the ability to receive an FDA cross- disciplinary project management team for interactive communications with senior managers and expert reviewers from FDA to expedite the development of a product. In December 2024** , we **announced completing our** ~~plan to request an~~ end- of- Phase 2 meeting with **the** FDA ~~during 2024~~ to ~~discuss a potential~~ **review and receive guidance on our proposed** Phase 3 **clinical** program for **a** future supplemental NDA **submission, or sNDA. We obtained FDA agreement on a proposed single Phase 3 study design for cytisinicline treatment in vaping cessation and on the additional requirements for submitting an sNDA, to expand cytisinicline for the treatment for vaping cessation. The FDA was in alignment on the proposed Phase 3 study design, including the inclusion / exclusion criteria, primary and secondary efficacy objectives, definition of vaping abstinence with biochemical verification, and other overall study assessments. The FDA agreed that one well- controlled Phase 3 trial, in addition to our completed Phase 2 ORCA- V1 trial and the safety exposure data from our ongoing ORCA- OL trial, would be sufficient for a vaping cessation indication as an sNDA** . Non- Clinical Program Supportive of IND and Phase 3 Clinical Development Non- clinical toxicology studies were sponsored by the NCCIH and by the NCI, to assist in our IND for investigating cytisinicline as a smoking cessation treatment. We filed this IND for cytisinicline with the FDA in 2017, which included the NCCIH sponsored non- clinical studies. Additional NCCIH and NCI sponsored non- clinical toxicology studies that evaluated reproductive toxicology were later submitted in support of our Phase 3 program. In December 2017, we initiated a series of drug metabolism, drug- to- drug interaction, and transporter studies of cytisinicline and results from these studies were announced in June 2018. These studies demonstrated that cytisinicline has no clinically significant interaction with any of the hepatic enzymes commonly responsible for drug metabolism nor clinically significant interaction with drug transporters. This suggests that cytisinicline may be administered with other medications without the need to modify the dose of any co- administered medications. In addition, company sponsored non- clinical toxicology studies that evaluated longer cytisinicline ~~treatment~~ **exposure** beyond one month to at least three months were submitted in 2020 prior to initiating our Phase 3 studies. Non- clinical toxicology studies that are required for **an** ~~a New Drug Application, or~~ NDA, including two longer- term chronic toxicology studies and two carcinogenicity studies, have been completed and submitted to the FDA. ~~Planned~~ **Ongoing** Company- Sponsored Clinical Trial ~~Planned~~ **Ongoing** Open Label ORCA- OL Trial ~~We plan to~~ **In May 2024 we** ~~initiate~~ **initiated** ~~an~~ **the ORCA- OL** open label exposure trial ~~,~~**. The trial is designed to provide long- term cytisinicline safety exposure data from subjects who currently**

smoke or use nicotine e- cigarettes and will receive cytisinicline treatment ~~or~~ **for up to one year. Cumulative 6- month exposure data from this study is required for submission of our cytisinicline NDA.** ORCA- OL ~~, in~~ **is designed to evaluate the long- term exposure of 3 mg cytisinicline treatment dosed** ~~the~~ **three** ~~second quarter of~~ **times daily in U. S. adults who want to quit smoking or vaping. In October** 2024 ~~and expect to~~ **, we announced that the trial completed enrollment of 479 subjects at 29 clinical trial sites across the United States. We** ~~enroll~~ **enrolled** subjects who **had** previously **participated in** ~~received cytisinicline as part of~~ the ORCA- program studies. **Participants were contacted to enroll in the** ORCA- OL ~~will recruit from the more than 1, 700 subjects who have participated in these prior trials, including more than 1, 100 who have already received cytisinicline treatment for either 6 or 12 weeks. Participants, whether they were previously using nicotine through smoking or vaping, will be encouraged to enroll in the~~ study if they ~~are~~ **were** currently using either, or both, **combustible cigarettes** ~~forms of smoking and /~~or **nicotine containing e- cigarettes (** vaping ~~nicotine~~ **)**. Subjects ~~will~~ receive cytisinicline treatment and ~~be~~ **are** monitored for safety events for up to one year. The primary endpoint is frequency of serious adverse events **, or SAEs**. Other safety and efficacy outcomes will be **collected** ~~assessed. The study is designed to enroll up to 650 subjects and is anticipated to start in the second quarter of 2024~~. Based on agreement with **the** FDA to follow ICH E1 guidance **for longer- term safety exposure for pharmaceuticals** , **results of** the **ORCA- OL trial are expected to meet the FDA requirement to provide safety data on a minimum of 300 subjects treated with cytisinicline for a cumulative period of six months as part of the anticipated** NDA submission ~~will include~~ **. Subsequently,** data **on** ~~from a minimum of 300 subjects who have received cumulative cytisinicline treatment for six months, and prior to potential approval, we will provide the FDA with data from~~ at least 100 subjects treated **for a total cumulative period of one year will be provided prior to potential product approval. ORCA- OL is being conducted at 29 clinical trial sites across the United States, all of which participated in previous ORCA- program clinical trials. In January 2025, we announced that the ORCA- OL trial had reached the goal of at least 300 subjects completing six months of cumulative cytisinicline treatment. The safety data from the 300 subjects treated** with cytisinicline for a cumulative ~~duration~~ **period** of ~~one year~~ **six months will be in included in our planned NDA submission at the end of the second quarter of 2025**. CLINICAL DEVELOPMENT PROGRAM Company- Sponsored Completed Phase 1 Trials Food Effect Phase 1 Trials In August 2017, we initiated our IND with a Phase 1 clinical study evaluating the effect of food on the bioavailability of cytisinicline in normal healthy volunteers. We completed the food effect study and announced the results in November of 2017 demonstrating similar bioavailability of cytisinicline in fed and fasted subjects. In 2018, Sopharma commercially launched a newly formulated cytisinicline tablet with improved shelf life in their territories. In May 2018, we initiated a study to evaluate the effect of food on the bioavailability of cytisinicline in volunteer smokers using this new formulation and data results were announced in September 2018. The study demonstrated similar bioavailability of cytisinicline in fed and fasted subjects. Cytisinicline was extensively absorbed after oral administration with maximum cytisinicline concentration levels observed in the blood within less than two hours with or without food. Total excretion levels of cytisinicline also remained equivalent in both the fed and fasted states. In 2023, we evaluated our planned commercial 3 mg formulated cytisinicline tablet in a 2- part Phase 1 clinical study with the first part evaluating the effect of food on the bioavailability of the 3 mg tablet in volunteer smokers. The study demonstrated similar bioavailability of cytisinicline in fed and fasted subjects and total excretion levels of cytisinicline also remained equivalent in both the fed and fasted states. In all Phase 1 Food Effect studies, cytisinicline was well tolerated. Other Phase 1 Safety Trials In October 2017, we initiated a clinical study assessing the repeat- dose PK and pharmacodynamics, or PD, effects of 1. 5 mg and 3 mg cytisinicline in 26 healthy volunteer smokers when administered over the 25- day downward titration regimen as marketed by Sopharma in their territories. Final results were presented at the Annual Meeting of the Society for Research on Nicotine and Tobacco, or SRNT, in February 2019. All 26 subjects completed the study. Predictable increases in plasma cytisinicline concentrations were observed with increasing unit dosing from 1. 5 mg to 3 mg. Smokers in the study were not required to have a designated or predetermined quit date. Overall, subjects had an 80 % reduction in cigarettes smoked, 82 % reduction in expired CO, and 46 % of the subjects achieved biochemically verified smoking abstinence by day 26. Subjects who received 3 mg cytisinicline over the 25 days had a trend for higher smoking abstinence compared to subjects who received 1. 5 mg cytisinicline. The AEs observed were mostly mild with transient headaches as the most commonly reported event. No serious adverse effects, or SAEs, were observed in the study. In March 2019, we initiated a clinical trial to evaluate the dose limiting AEs that would define the maximum tolerated dose, or MTD, for a single administered oral dose of cytisinicline. This study evaluated smokers who received one single dose of cytisinicline. The starting dosage of cytisinicline was 6 mg and was to be increased in separate groups of subjects for each escalated dose level until **defined** stopping criteria (based on the occurrence of dose- limiting AEs) were reached. A safety review after each dose level was performed by an independent Data Safety Monitor Committee, or DSMC, before escalation to the next dose level. Six dose levels were pre- planned with 21 mg cytisinicline as the highest dose level. When the MTD was not reached at 21 mg, the study was amended to evaluate doses up to 30 mg, as recommended by the DSMC. At this 30 mg dose, the stopping criteria of ~~serious or severe~~ **dose- limiting** AEs were still not met, but the DSMC recommended stopping the study since the frequency of gastrointestinal symptoms were approaching an MTD level. The results were reviewed with the FDA, with an agreement that further escalation beyond the single 30 mg dose was not required. This Phase- 1 study fulfills an FDA requirement to evaluate potential safety issues in the event patients exceed a recommended single dose outside of a clinical trial setting. Three additional Phase 1 clinical studies were conducted in 2022 and 2023 for the NDA: one pharmacokinetics, or PK, study to evaluate for any increased cytisinicline blood levels in subjects who have various levels of renal impairment; another PK study to determine various remaining PK parameters for the 3 mg TID cytisinicline regimen, including the timing of steady state dosing; and a cardiac safety study to evaluate for any effects of cytisinicline on QT interval prolongation. All 3 studies have been completed. The renal impairment study demonstrated that cytisinicline is excreted unchanged in urine and the pharmacokinetics of cytisinicline are dependent on renal function. Cytisinicline was generally observed to be well tolerated in subjects with varying degrees of renal impairment compared to subjects with normal renal function. The PK study demonstrated

that the 3mg cytisinicline TID dosing regimen reached steady state cytisinicline pharmacokinetics by the second day of TID administration. The cardiac safety QT / QTc study evaluating therapeutic and supratherapeutic high doses of cytisinicline demonstrated that cytisinicline has no clinically relevant effect on QT interval prolongation or cardiac repolarization. Company-Sponsored Completed Phase 2 Trials Phase 2b ORCA- 1 Trial for Smoking Cessation We conducted the Phase 2b ORCA- 1 dose selection trial, which was initiated in October 2018 and evaluated 254 smokers in the United States. The trial evaluated both 1. 5 mg and 3 mg doses of cytisinicline on the standard declining titration schedule as well as a more simplified TID dosing schedule, both over 25 days. The trial was randomized and blinded to compare the effectiveness of the cytisinicline doses and schedules to respective placebo groups. All subjects were treated for 25 days, provided behavioral support, and followed up for an additional four weeks to assess smoking abstinence. The primary endpoint in the study was the reduction in daily smoking, a self- reported measure. Three of the four cytisinicline treatment arms demonstrated a statistically significant ~~reduction~~ **improvement** , p < 0. 05, compared to placebo **. The fourth arm trended to significance (p = 0. 052)** . Across all treatment arms, over the 25- day treatment period, subjects on cytisinicline experienced a 74- 80 % median reduction in the number of cigarettes smoked, compared to a 62 % reduction in the placebo arms. The ~~primary endpoint in the study was the reduction in daily smoking, a self- reported measure. Three of the four cytisinicline treatment arms demonstrated a statistically significant improvement, p < 0. 05, compared to placebo. The fourth arm trended to significance (p = 0. 052). Across all treatment arms, over the 25- day treatment period, subjects on cytisinicline experienced a 74- 80 % median reduction in the number of cigarettes smoked, compared to a 62 % reduction in the placebo arms. The~~ secondary endpoint of the trial was a 4- week continuous abstinence rate, which is the **more** relevant endpoint for regulatory approval. All cytisinicline treatment arms showed significant improvements in abstinence rates compared to the placebo arms. Notably, the 3 mg TID cytisinicline arm demonstrated a 50 % abstinence rate at week 4, compared to 10 % for placebo (p < 0. 0001) and a continuous abstinence rate, weeks 5 through 8, of 30 % for cytisinicline compared to 8 % for placebo (p = 0. 005). Smokers in the 3 mg TID arm had an **Odds Ratio, or** OR **,** of 5. 04 (95 % CI: 1. 42, 22. 32) for continuous abstinence from week 5 to week 8, compared with placebo, meaning, smokers receiving 3 mg cytisinicline TID were five times more likely to stop smoking compared to smokers receiving placebo. At week 4, all four cytisinicline arms **also** demonstrated statistically significant (p < 0. 05) reductions in expired carbon monoxide, or CO, a biochemical measure of smoking activity. Expired CO levels had declined by a median of 71- 80 % in the cytisinicline treatment arms, compared to only 38 % in the placebo arms. Cytisinicline was well- tolerated with no SAEs reported. The most commonly reported (> 5 %) **adverse events, or** AEs **,** across all cytisinicline treatment arms versus placebo arms were abnormal dreams, insomnia, upper respiratory tract infections, and nausea. In the 3 mg TID treatment arm versus placebo arms, the most common AEs were abnormal dreams, insomnia, and constipation (each 6 % vs 2 %), upper respiratory tract infections (6 % vs 14 %), and nausea (6 % vs 10 %), respectively. Compliance with study treatment was greater than 94 % across all arms. A summary of AEs reported in subjects in the ORCA- 1 trial is included in the table below. TID Declining Titration Pooled 1. 5 mg (n = 52) 3. 0 mg (n = 50) 1. 5 mg (n = 51) 3. 0 mg (n = 50) Cytisinicline (n = 203) Placebo (n = 51) At least 1 AE 20 (39 %) 21 (42 %) 29 (57 %) 23 (46 %) 93 (46 %) 24 (47 %) URTI 5 (10 %) 3 (6 %) 3 (6 %) 2 (4 %) 13 (6 %) 7 (14 %) Abnormal dreams 4 (8 %) 3 (6 %) 4 (8 %) 7 (14 %) 18 (9 %) 1 (2 %) Nausea 1 (2 %) 3 (6 %) 5 (10 %) 3 (6 %) 12 (6 %) 5 (10 %) Insomnia 4 (8 %) 3 (6 %) 3 (6 %) 4 (8 %) 14 (7 %) 1 (2 %) Headache 6 (12 %) 2 (4 %) 1 (2 %) 1 (2 %) 10 (5 %) 2 (4 %) Fatigue 3 (6 %) 1 (2 %) 1 (2 %) 2 (4 %) 7 (3 %) 2 (4 %) Constipation 1 (2 %) 3 (6 %) 0 (0 %) 0 (0 %) 4 (2 %) 1 (2 %) The outcome of the ORCA- 1 trial was the selection of 3 mg TID for Phase 3 development. Overall, the 3 mg dose administered TID demonstrated the best overall safety and efficacy when compared to other doses and administrations studies in ORCA- 1. The results from ORCA- 1 study were published in the journal Nicotine and Tobacco Research in 2021. Phase 2 ORCA- V1 Trial for E- cigarette (Vaping) Cessation In June 2022, following NIDA / NIH review of completed regulatory and clinical operational milestones plus acceptance of the IND by **the** FDA, we announced that we were awarded the next grant funding from NIDA in the amount of approximately $ 2. 5 million. The full grant award of $ 2. 8 million covered approximately half of the total ORCA- V1 clinical study costs. The Primary Investigators for the grant ~~are~~ **were Dr. Cindy Jacobs,** our President and Chief Medical Officer ~~, Dr. Cindy Jacobs~~ , and Dr. Nancy Rigotti, Professor of Medicine at Harvard Medical School and Director, Tobacco Research and Treatment Center, Massachusetts General Hospital. In June 2022, we announced the initiation of the Phase 2 ORCA- V1 clinical trial. In April 2023, we reported positive topline results showing a statistically significant vaping cessation benefit for cytisinicline- treated participants in the ORCA- V1 trial. ORCA- V1 evaluated 160 adults who used e- cigarettes on a daily basis at five clinical trial locations in the United States. ORCA- V1 participants were randomized to receive 3 mg cytisinicline three times daily or placebo for 12 weeks in combination with standard cessation behavioral support. The primary endpoint for ORCA- V1 was biochemically verified continuous abstinence from nicotine e- cigarette use, measured during the last 4 weeks of treatment. Subjects who received 12 weeks of cytisinicline treatment had 2. ~~6~~ **64** times higher odds, or likelihood, to have quit vaping during the last four weeks of treatment compared to subjects who received placebo (p = 0. ~~035~~ **04**). The vaping cessation rate during weeks 9 through 12 was 31. 8 % for cytisinicline compared to 15. 1 % for placebo. A benefit in favor of cytisinicline was consistently observed across the secondary endpoints. Additionally, a cessation benefit was observed for cytisinicline across clinical trial sites and participant demographics such as age, gender, race, or whether they had smoked cigarettes in the past. Cytisinicline was well tolerated and no SAEs were reported. Similar rates of AEs were observed between treatment arms (54. 7 % in the placebo arm vs. 50. 9 % in the cytisinicline arm). The most commonly reported (> 5 %) AEs in the placebo arm, in order of frequency, were nausea, COVID- 19 infection, headache, anxiety, and upper respiratory tract infection. In the cytisinicline arm, > 5 % AEs reported, in order of frequency, were sleep disturbances, anxiety, headache, fatigue, and upper respiratory tract infection. ORCA- V1 trial results were presented at the **Society for Research on Nicotine and Tobacco, or** SRNT **,** European ~~annual~~ **Annual** ~~meeting~~ **Meeting** in September 2023 ~~and~~ **,** the SRNT ~~US~~ **U. S.** ~~annual~~ **Annual** ~~meeting~~ **Meeting** in March **2024, the Society of General Internal Medicine U. S. Annual Meeting in May 2024 and final study results were published in the Journal of the American Medical Association, or JAMA, Internal Medicine in**

May 2024. Company- Sponsored Phase 3 Clinical Trials for Smoking Cessation Indication Completed Phase 3 ORCA- 2 Trial In April 2022, we announced positive topline results for the Phase 3 ORCA- 2 clinical trial. ORCA- 2 was initiated in October 2020 and evaluated the efficacy and safety of 3 mg cytisinicline dosed three times daily compared to placebo in 810 adult smokers at 17 clinical sites in the United States. ORCA- 2 participants were randomized to one of three study arms to determine the smoking cessation efficacy and safety profile of cytisinicline when administered for either 6 or 12 weeks, compared to placebo. All subjects received standard behavioral support and were assigned to one of the following groups: • Arm A: 12 weeks of placebo • Arm B: 6 weeks of cytisinicline, followed by 6 weeks of placebo • Arm C: 12 weeks of cytisinicline The ORCA- 2 study had two independent primary endpoints that evaluated for successful smoking cessation for both 6- week and 12- week durations of cytisinicline treatment, compared to placebo. The primary endpoints for ORCA- 2 were biochemically verified continuous smoking cessation measured during the last 4 weeks of each treatment duration. Both the 6- and 12- week cytisinicline treatments demonstrated significantly better quit rates than placebo with ~~odds ratios, or~~ ORs ~~,~~ of 8. 0 and 6. 3, respectively. • Subjects who received 12 weeks of cytisinicline treatment had 6. 3 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p < 0.0001$). The abstinence rate during weeks 9- 12 was 32. 6 % for cytisinicline compared to 7. 0 % for placebo. • Subjects who received 6 weeks of cytisinicline treatment had 8. 0 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p < 0.0001$). The abstinence rate during weeks 3- 6 was 25. 3 % for cytisinicline compared to 4. 4 % for placebo. The secondary endpoints measured continuous smoking abstinence after treatment out to 24 weeks. Both the 6- and 12- week secondary endpoints for continuous abstinence demonstrated significantly better quit rates for cytisinicline treated subjects than placebo. The continuous abstinence rate from week 9 to 24 was 21. 1 % for the 12- week cytisinicline arm compared to 4. 8 % for placebo, with an OR of 5. 3 ($p < 0.0001$). The continuous abstinence rate from week 3 to 24 was 8. 9 % for the 6- week cytisinicline arm compared to 2. 6 % for placebo, with an OR of 3. 7 ($p = 0.0016$). A third secondary endpoint compared the two cytisinicline treatment arms and evaluated for an increased risk in relapse from week 6 to week 24 when subjects were switched to placebo during week 6 to week 12 (Arm B) instead of receiving cytisinicline for another 6 weeks during week 6 to week 12 (Arm C). The analysis showed that there was no increased risk of smoking relapse in subjects who had successfully quit smoking by week 3 through week 6 if they received placebo instead of continuing cytisinicline from week 6 to week 12. Cytisinicline was well tolerated with no treatment- related **SAEs** ~~serious adverse events~~ reported. The most commonly reported **AEs** ~~adverse events~~ (occurring greater than 5 % overall in the study) for placebo, 6- week cytisinicline, and 12- week cytisinicline ~~, respectively, were~~ **are shown in the following table** : Placebo 6- Weeks Cytisinicline 12- Weeks CytisiniclineInsomnia 4. 8 % 8. 6 % 9. 6 % Abnormal Dreams 3. 0 % 8. 2 % 7. 8 % Headaches 8. 1 % 6. 7 % 7. 8 % Nausea 7. 4 % 5. 9 % 5. 6 % Additional analyses from the ORCA- 2 trial were presented at the ~~Society for Research on Nicotine and Tobacco, or~~ SRNT ~~,~~ annual meeting in March 2023 and final study results were published in ~~the Journal of the American Medical Association, or~~ JAMA ~~,~~ in July 2023. Completed Phase 3 ORCA- 3 Trial In May 2023, we announced positive topline results for our Phase 3 ORCA- 3 clinical trial. ORCA- 3 was initiated in January 2022 and was a confirmatory Phase 3 trial required for registrational approval of cytisinicline in the United States and had the same design as the Phase 3 ORCA- 2 trial. This Phase 3 trial evaluated the efficacy and safety of 3 mg cytisinicline dosed three times daily compared to placebo in 792 adult smokers at 20 clinical sites. ORCA- 3 participants were randomized to one of three study arms to evaluate cytisinicline administered for either 6 or 12 weeks, compared to placebo. All subjects received standard behavioral support and were assigned to one of the following groups: The primary outcome measure of success in the ORCA- 3 trial was biochemically verified continuous smoking cessation during the last four weeks of treatment in the 6 and 12- week cytisinicline treatment arms compared with placebo. Each treatment arm was compared independently to the placebo arm. Secondary outcome measures were conducted to assess continued smoking abstinence rates through six months from the start of study treatment. Primary endpoint: • Subjects who received 12 weeks of cytisinicline treatment had 4. 4 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p < 0.0001$). The smoking cessation rate during weeks 9 through 12 was 30. 3 % for cytisinicline compared to 9. 4 % for placebo. • Subjects who received 6 weeks of cytisinicline treatment had 2. 85 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p = 0.0008$). The smoking cessation rate during weeks 3 through 6 was 14. 8 % for cytisinicline compared to 6 % for placebo. Secondary endpoint: • The continuous smoking cessation rate from week 9 to week 24 was 20. 5 % for the 12- week cytisinicline arm compared to 4. 2 % for placebo, with an odds ratio of 5. 79 ($p < 0.0001$). • The continuous smoking cessation rate from week 3 to week 24 was 6. 8 % for the 6- week cytisinicline arm compared to 1. 1 % for placebo, with an odds ratio of 6. 25 ($p = 0.0006$). The third secondary endpoint compared the two cytisinicline treatment arms for an increased risk in relapse from week 6 to week 24 when subjects were switched to placebo during week 6 to week 12 (Arm B) instead of receiving cytisinicline for another 6 weeks during week 6 to week 12 (Arm C). The analysis showed that there was no increased risk of smoking relapse in subjects who had successfully quit smoking by week 3 through week 6 and switched to placebo. ORCA- 3 subjects had an average age of 53 years, smoked a median of 20 cigarettes per day at baseline, and had a median smoking history of 36 years with 4 prior quit attempts. Similar to ORCA- 2 findings, cytisinicline was well- tolerated with no treatment- related **SAEs** ~~serious adverse events~~ reported. The most commonly reported (> 5 % overall) **AEs** ~~adverse events~~ for placebo, 6- week cytisinicline, and 12- week cytisinicline ~~were~~ **are shown in the following table** : Placebo 6- Weeks Cytisinicline 12- Weeks CytisiniclineInsomnia 7. 6 % 11. 0 % 11. 9 % Abnormal Dreams 5. 7 % 9. 1 % 7. 7 % Nausea 7. 3 % 9. 5 % 6. 9 % Headaches 6. 1 % 7. 6 % 8. 5 % ~~Other Investigator- Sponsored Clinical Trials In June 2020, we announced the topline results from the independent, investigator- sponsored Phase 3 RAUORA trial. RAUORA was a non- inferiority study comparing cytisinicline to Chantix (varenicline) in Māori (indigenous New Zealanders) and whānau (family) of Māori. The study was led by Dr. Natalie Walker, Associate Professor at the University of Auckland, and was funded by the Health Research Council of New Zealand. The study enrollment was planned for 2, 140 subjects. In total, 1, 105 Māori or~~

~~whānau expressed interest in participating in the study and a total of 679 were randomized to receive either cytisinicline or varenicline. The average age of participants in the trial was 43 years and approximately 70 % of the participants were women. The study compared 1. 5 mg tablets of cytisinicline administered on a schedule of 25 days of declining titration followed by twice- daily dosing for a total of 12 weeks with varenicline administered on a schedule of seven days of inclining titration followed by twice- daily dosing for a total of 12 weeks. The primary endpoint was a comparison of biochemically confirmed continuous abstinence rates at six months, and the trial was designed to assess if the two agents were non- inferior to each other. The primary endpoint of the non- inferiority trial was to demonstrate that cytisinicline quit rates would be no less than 10 % lower than the quit rates for varenicline. Topline results indicated that the RAUORA trial achieved its primary endpoint in showing that cytisinicline plus behavioral support was at least as effective as varenicline plus behavioral support at 6 months. Cytisinicline met the pre- specified non- inferiority endpoint and was trending towards superiority with an Absolute Risk Difference of 4. 29 in favor of cytisinicline (95 % CI- 0. 22 to 8. 79), demonstrating a 4. 29 % improvement in quit rates in favor of cytisinicline. Specifically, continuous abstinence rates at 6 months, verified by expired CO, were 12. 1 % for cytisinicline compared to 7. 9 % for varenicline. The Relative Risk was 1. 55 on an intent- to- treat basis, indicating that subjects in the cytisinicline arm were approximately one and a half times more likely to have quit smoking at 6 months compared to subjects who received varenicline. Additionally, significantly fewer overall AEs were reported in cytisinicline- treated subjects (Relative Risk 0. 56, 95 % CI 0. 49 to 0. 65, p < 0. 001). Notably, of the subjects who experienced adverse events, cytisinicline subjects reported significantly less nausea, insomnia and vivid dreams (p < 0. 05). The final RAUORA trial results and additional analyses were presented at the SRNT European Annual Meeting in September 2020 and were published in the journal Addiction in March 2021.~~ OVERVIEW OF SMOKING CESSATION MARKET AND TREATMENT OPTIONS Overview of the Tobacco Epidemic Smoking remains the leading cause of preventable death worldwide and in the United States. The World Health Organization, or WHO, estimates that there are approximately 1. 3 billion tobacco users globally and that tobacco kills more than 8 million people each year. More than 7 million of those deaths are the result of direct tobacco use, while around 1. 3 million are the result of non- smokers being exposed to second- hand smoke. In the United States alone, cigarette smoking is responsible for more than 480, 000 deaths every year, or about one in five deaths. The Centers for Disease Control and Prevention, or CDC, estimates that the annual cost of smoking related illnesses in the United States is more than $ 600 billion in direct medical care and lost productivity. Over 16 million people in the United States are living with a disease caused by smoking. Among these diseases are cancer, heart disease, stroke, lung diseases, diabetes and chronic obstructive pulmonary disease which includes emphysema and chronic bronchitis. Smoking also increases risk for tuberculosis, certain eye diseases and problems of the immune system, including rheumatoid arthritis. More than 87 % of lung cancer deaths, 61 % of all pulmonary disease deaths, and 32 % of all deaths from coronary heart disease are attributable to smoking and exposure to secondhand smoke according to the CDC. Tobacco smoking is highly addictive, and research suggests that nicotine may be as addictive as heroin, cocaine and alcohol. The CDC estimates that more people in the United States are addicted to nicotine than any other drug and reports that, historically, nearly 70 % of smokers desired to quit and 55 % made an attempt to do so in the prior year. Despite the high number of attempts, fewer than one in ten people are successful in their attempt to quit each year. Additionally, up to 60 % of people who quit smoking relapse in the first year. One increasingly popular alternative to smoking is the use of e- cigarettes, or vaping, which deliver liquid nicotine into a mist or vapor which is inhaled. This method of consumption avoids the chemicals that are associated with cigarette smoke but may have other associated health and safety issues. The emerging use of e- cigarettes is contributing to the growing population of people who are addicted to nicotine. According to data from the National Health Interview Survey, published by the CDC in May 2023, it is estimated that more than 11 million adults in the United States used e- cigarettes in 2021. **A** ~~In a~~ study that we conducted and that was presented at the 2021 SRNT Annual Meeting, **showed results from** surveying approximately 500 users of nicotine vaping devices or e- cigarettes ~~,~~ **with** approximately 73 % of participants ~~responded~~ **responding** that they intend to quit vaping within the next three to 12 months. Of those who intended to quit even sooner, within the next 3 months, more than half stated they would be extremely likely to try a new prescription product to help them do so. Further, survey data published in JAMA Network Open in 2021, found that 61 % of adult vape users overall endorsed future plans to quit. Intentions to quit were highest, reported at 66 %, in those survey participants who were former cigarette smokers and currently using vape devices **. We believe that cytisinicline, if approved, could be the first prescription drug indicated for vape and e- cigarette users who are ready to quit their nicotine dependence** . Overview of Smoking Cessation Marketplace & Treatments According to DelveInsight' s 2020 report " Smoking Cessation Market Insights, Epidemiology and Market Forecast ", global revenues for prescription smoking cessation therapies are estimated to reach $ 5. 6 billion by 2030. In 2023, approximately 8 million prescriptions were written for smoking cessation in the United States alone. Only two non- nicotine, prescription treatments for smoking cessation are currently available in the United States: " varenicline " (formerly marketed by Pfizer as Chantix) and " bupropion " (formerly marketed by GlaxoSmithKline as Zyban). Both are currently available as generic formulations. Varenicline requires a **minimum** three- month treatment period and bupropion is recommended for a period between seven and 12 weeks. While both have been proven effective in aiding smoking cessation, they are also associated with significant side effects and early discontinuations from treatment. Varenicline' s labeling indicates elevated instances of nausea, abnormal dreams, constipation, flatulence, and vomiting may be experienced by varenicline- treated patients compared to placebo- treated patients, and buproprion' s product label discloses potential adverse reactions including insomnia, rhinitis, dry mouth, dizziness, nervous disturbance, anxiety, nausea, constipation, arthralgia and seizures. High uptake into the brain combined with activity at " off target " receptors could be responsible for varenicline' s adverse event profile. In June 2021, Pfizer Inc. halted the distribution of Chantix **(varenicline)** after heightened levels **of a nitrosamine impurity** , **called N- nitroso- varenicline, which were** above the FDA' s acceptable daily intake limit, ~~of nitrosamines~~ were found in some lots of Chantix pills **. Long- term use of products with N- nitroso- varenicline may be associated with a potential increased cancer risk in humans** . In September 2021, Pfizer announced a

nationwide recall in the United States of all lots of Chantix and have also withdrawn the product in other countries around the globe. Prior to market withdrawal and launch of generic Chantix (varenicline), global sales of branded Chantix peaked at $ 1. 1 billion. Of those sales, approximately 75 % were attributable to the U. S. market. The vast majority of OTC smoking cessation aids are NRTs. NRTs come in many forms, including gums, lozenges and patches, and have been shown to be less effective than prescription drugs. For example, a Cochrane Group independent database review of nicotine receptor partial agonists published in 2016 compared varenicline with a number of NRTs and varenicline has been proven to be more effective than the NRTs, as demonstrated in head- to- head studies. We believe that cytisinicline represents a unique opportunity to significantly impact global health by addressing the considerable unmet need among millions of smokers and e- cigarettes users. If approved by the FDA, it stands to become the first new prescription medicine in nearly two decades aimed at aiding individuals in overcoming nicotine dependence. With its product profile, cytisinicline is positioned to offer a novel solution characterized by robust efficacy ~~and a lack of~~ **in our clinical trials, without the** burdensome side effects ~~in our clinical trials,~~ which have hindered compliance and adoption with current treatments. Additionally, its dosing flexibility with a 6 or 12- week regimen, along with its natural derivation, is perceived favorably by certain potential patients. LICENSE & SUPPLY AGREEMENTS In 2009 and 2010, we entered into a license agreement, or the Sopharma License Agreement, and a supply agreement, or the Sopharma Supply Agreement, with Sopharma. Pursuant to the Sopharma License Agreement, we were granted access to all available manufacturing, efficacy and safety data related to cytisinicline, as well as a granted patent in several European countries including Germany, France and Italy related to oral dosage forms of cytisinicline. Additional rights granted under the Sopharma License Agreement include the exclusive use of, and the right to sublicense, the trademark Tabex in all territories — other than certain countries in Central and Eastern Europe, Scandinavia, North Africa, the Middle East and Central Asia, as well as Vietnam, where Sopharma or its affiliates and agents already market Tabex — in connection with the marketing, distribution and sale of products. Under the Sopharma License Agreement, we agreed to pay a nonrefundable license fee. In addition, we agreed to make certain royalty payments equal to a mid- teens percentage of all net sales of Tabex branded products in our territory during the term of the Sopharma License Agreement, including those sold by a third party pursuant to any sublicense which may be granted by us. We have agreed to cooperate with Sopharma in the defense against any actual or threatened infringement claims with respect to Tabex. Sopharma has the right to terminate the Sopharma License Agreement upon the termination or expiration of the Sopharma Supply Agreement. The Sopharma License Agreement will also terminate under customary termination provisions including bankruptcy or insolvency and material breach. To date, any amounts paid to Sopharma pursuant to the Sopharma License Agreement have been immaterial. A cross- license exists between us and Sopharma whereby we grant to Sopharma rights to any patents or patent applications or other intellectual property rights filed by us in Sopharma territories. On May 14, 2015, we and Sopharma entered into an amendment to the Sopharma License Agreement. Among other things, the amendment to the Sopharma License Agreement reduced the royalty payments payable by us to Sopharma from a percentage in the mid- teens to a percentage in the mid- single digits and extended the term of the Sopharma License Agreement until May 26, 2029. On July 28, 2017, we and Sopharma entered into the amended and restated Sopharma Supply Agreement. Pursuant to the amended and restated Sopharma Supply Agreement, for territories as detailed in the licensing agreement, we will exclusively purchase all of our cytisinicline from Sopharma, and Sopharma agrees to exclusively supply all such cytisinicline requested by us, and we extended the term to 2037. In addition, we will have full access to the cytisinicline supply chain and Sopharma will manufacture sufficient cytisinicline to meet a forecast for a specified demand of cytisinicline for the five years commencing shortly after the commencement of the agreement, with the forecast to be updated regularly thereafter. Each of us and Sopharma may terminate the Sopharma Supply Agreement in the event of the other party' s material breach or bankruptcy or insolvency. Share Purchase Agreement On May 14, 2015, we entered into a Share Purchase Agreement with Sopharma ~~AD~~ to acquire 75 % of the outstanding shares of Extab Corporation for $ 2. 0 million in cash and $ 2. 0 million in a deferred payment, contingent on regulatory approval of cytisinicline by the FDA or the European Medicines Agency ~~, or EMA~~. The fair value of the contingent consideration on the acquisition date was nil. The contingent consideration liability is measured at fair value in our financial statements ~~. As of December 31, 2023, the fair value of the contingent consideration was estimated to be $ 0. 5 million~~ (see Note 2 ~~"~~ **“** Significant Accounting Policies, Sopharma Share Purchase Agreement Contingent Consideration ~~"~~ **“** in the accompanying consolidated Financial Statements) ~~. We recognized a loss of $ 0. 5 million for the year ended December 31, 2023~~. University of Bristol In July 2016, we entered into a license agreement with the University of Bristol, or the University of Bristol License Agreement. Under the University of Bristol License Agreement, we received exclusive and nonexclusive licenses from the University of Bristol to certain patent and technology rights resulting from research activities into cytisinicline and its derivatives for use in smoking cessation, including a number of patent applications related to novel approaches to cytisinicline binding at the nicotinic receptor level. Any patents issued in connection with these applications would be scheduled to expire on February 5, 2036, at the earliest. In consideration of rights granted by the University of Bristol, we agreed to pay amounts of up to $ 3. 2 million, in the aggregate, tied to a financing milestone and to specific clinical development and commercialization milestones resulting from activities covered by the University of Bristol License Agreement. Additionally, if we successfully commercialize product candidates subject to the University of Bristol License Agreement, we are responsible for royalty payments in the low- single digits and payments up to a percentage in the mid- teens of any sublicense income, subject to specified exceptions, based upon net sales of such licensed products. On January 22, 2018, we and the University of Bristol entered into an amendment to the University of Bristol License Agreement. Pursuant to the amended University of Bristol License Agreement, we received exclusive rights for all human medicinal uses of cytisinicline across all therapeutic categories from the University of Bristol from research activities into cytisinicline and its derivatives. In consideration of rights granted by the amended University of Bristol License Agreement, we agreed to pay an initial amount of $ 37, 500 upon the execution of the amended University of Bristol License Agreement, and additional amounts of up to $ 1. 7 million, in the aggregate, tied to a financing milestone and to specific clinical development and commercialization

milestones resulting from activities covered by the amended University of Bristol License Agreement, in addition to amounts under the original University of Bristol License Agreement of up to $ 3. 2 million in the aggregate, tied to specific financing, development and commercialization milestones. Additionally, if we successfully commercialize any product candidate subject to the amended University of Bristol License Agreement or to the original University of Bristol License Agreement, we will be responsible, as provided in the original University of Bristol License Agreement, for royalty payments in the low- single digits and payments up to a percentage in the mid- teens of any sublicense income, subject to specified exceptions, based upon net sales of such licensed products. Up to December 31, ~~2023~~ **2024** , we had paid the University of Bristol $ 125, 000 pursuant to the University of Bristol License Agreement. Unless otherwise terminated, the University of Bristol License Agreement will continue until the earlier of July 2036 or the expiration of the last patent claim subject to the University of Bristol License Agreement. We may terminate the University of Bristol License Agreement for convenience upon a specified number of days' prior notice to the University of Bristol. The University of Bristol License Agreement will terminate under customary termination provisions including bankruptcy or insolvency or its material breach of the agreement. Under the terms of the University of Bristol License Agreement, we had provided 100 grams of cytisinicline to the University of Bristol as an initial contribution. Summary of Milestone and Contingent Obligations by Product Candidate The following table sets forth the milestones and contingent obligations that we may be required to pay to third parties under the license and share purchase agreements described above. As described above, we will also be required to pay certain revenue- based royalties with respect to our product candidate. Milestone Obligations to Third Parties Amount Payable University of Bristol Up to $ 4, 837, 500 (1) Sopharma AD $ 2, 000, 000 (2) (1) Payable in connection with specific financing, development and commercialization milestones. (2) Payable contingent on regulatory approval by the FDA or EMA. GOVERNMENT REGULATIONS We are heavily regulated in most of the countries in which we operate. In the United States, the principal regulating authority is the FDA. The FDA regulates the safety and efficacy of product candidates and research, quality, manufacturing processes, product approval and promotion, advertising and product labeling. In the EU, the EMA and national regulatory agencies regulate the scientific evaluation, supervision and safety monitoring of product candidates, and oversee the procedures for approval of drugs for the EU and European Economic Area, or EEA, countries similar regulations exist in most other countries, and in many countries the government also regulates prices. Health authorities in many middle- and lower- income countries require marketing approval by a recognized regulatory authority, such as the FDA or EMA, before they begin to conduct their application review process and / or issue their final approval. ~~We intend to focus initially on clinical development and regulatory approval of cytisinicline in the United States.~~ It is anticipated that cytisinicline tablets ~~would~~ **could** receive **up to seven and** a **half** ~~minimum five~~ years of data exclusivity under the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch- Waxman Act. Before a new pharmaceutical product may be marketed in the United States, the FDA must approve an NDA for a new drug. The steps required before the FDA will approve an NDA generally include non- clinical studies followed by multiple stages of clinical trials conducted by the trial sponsor; sponsor submission of the NDA ~~application~~ to the FDA for review; the FDA' s review of the data to assess the drug' s safety and effectiveness; and the FDA' s inspection of the facilities where the product will be manufactured. As a condition of product approval, the FDA may require a sponsor to conduct post-marketing clinical trials, known as Phase 4 trials, and surveillance programs to monitor the effect of the approved product. The FDA may limit further marketing of a product based on the results of these post- market trials and programs. Any modifications to a drug, including new indications or changes to labeling or manufacturing processes or facilities, may require the submission and approval of a new or supplemental NDA before the modification can be implemented, which may require that we generate additional data or conduct additional non- clinical studies and clinical trials. Our ongoing manufacture and distribution of drugs is subject to continuing regulation by the FDA, including recordkeeping requirements, reporting of adverse experiences associated with the product, and adherence to current Good Manufacturing Practices, or cGMPs, which regulate all aspects of the manufacturing process. We are also subject to numerous regulatory requirements relating to the advertising and promotion of drugs, including, but not limited to, standards and regulations for direct- to- consumer advertising. Failure to comply with the applicable regulatory requirements governing the manufacture and marketing of our products may subject us to administrative or judicial sanctions, including warning letters, product recalls or seizures, injunctions, fines, civil penalties and / or criminal prosecution. Sales and Marketing. The marketing practices of U. S. pharmaceutical companies are generally subject to various federal and state healthcare laws that are intended to prevent fraud and abuse in the healthcare industry and protect the integrity of government healthcare programs. These laws include anti- kickback laws and false claims laws. Anti- kickback laws generally prohibit a biopharmaceutical or medical device company from soliciting, offering, receiving or paying any remuneration to generate business, including the purchase or prescription of a particular product. False claims laws generally prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for payment for reimbursed drugs or services to third- party payors (including Medicare and Medicaid) that are false or fraudulent. Although the specific provisions of these laws vary, their scope is generally broad and there may not be regulations, guidance or court decisions that apply the laws to any particular industry practices, including the marketing practices of pharmaceutical and medical device companies. Violations of fraud and abuse laws may be punishable by criminal or civil sanctions and / or exclusion from federal healthcare programs (including Medicare and Medicaid). The U. S. federal government and various states have also enacted laws to regulate the sales and marketing practices of pharmaceutical or medical device companies. These laws and regulations generally limit financial interactions between manufacturers and healthcare providers; require disclosure to the federal or state government and public of such interactions; and / or require the adoption of compliance standards or programs. Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Given the lack of clarity in laws and their implementation, our activities could be subject to penalties under the pertinent laws and regulations. Healthcare Reform. The United States and state governments continue to propose and pass legislation designed to regulate the healthcare industry. In March 2020, the Patient Protection and Affordable Care Act, or ACA, as amended by the Healthcare and

Education Reconciliation Act, or collectively, the Healthcare Reform Law, was passed and included changes that significantly affected the pharmaceutical industry, such as: • Increasing drug rebates paid to state Medicaid programs under the Medicaid Drug Rebate Program for brand name and generic prescription drugs and extending those rebates to Medicaid managed care; • Requiring pharmaceutical manufacturers to provide discounts on brand name prescription drugs sold to Medicare beneficiaries whose prescription drug costs cause the beneficiaries to be subject to the Medicare Part D coverage gap; and • Imposing an annual fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. The ACA includes provisions designed to increase the number of Americans covered by health insurance. Specifically, since 2014, the ACA has required most individuals to maintain health insurance coverage or potentially to pay a penalty for noncompliance and has offered states the option of expanding Medicaid coverage to additional individuals. Additionally, policy efforts designed specifically to reduce patient out- of- pocket costs for medicines could result in new mandatory rebates and discounts or other pricing restrictions. Adoption of other new legislation at the federal or state level could further affect demand for, or pricing of, our products. Pricing and Reimbursement. Pricing for our pharmaceutical products will depend in part on government regulation. We will likely be required to offer discounted pricing or rebates on purchases of pharmaceutical products under various federal and state healthcare programs, such as the Medicaid Drug Rebate Program, the " federal ceiling price " drug pricing program, the 340B drug pricing program and the Medicare Part D Program. We will also be required to report specific prices to government agencies under healthcare programs, such as the Medicaid Drug Rebate Program and Medicare Part B. The calculations necessary to determine the prices reported are complex and the failure to report prices accurately may expose us to penalties. In the United States, Medicaid currently covers all smoking cessation products including varenicline and bupropion. The ACA substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U. S. pharmaceutical industry. Section 2502 of the ACA specifies that tobacco cessation medications will be removed from the list of optional medications and required for inclusion in states' prescription drug benefit. On May 2, 2014 the Department of Health and Human Services, or HHS, provided guidance into insurance coverage policy that health plans would be in compliance if they cover, among other items, screening for tobacco use, individual, group and phone counseling, all FDA approved tobacco cessation medications (both prescription and OTC) when prescribed by a healthcare provider, at least two quit attempts per year, four sessions of counseling and 90 days of treatment, with no cost sharing (co- pay) required. Government and private third- party payers routinely seek to manage utilization and control the costs of our products. For example, private third- party payers and the majority of states use preferred drug lists to restrict access to certain pharmaceutical products under both of these types of payer types. Private third- party payers are constantly under healthcare budgetary constraints and utilize Pharmacy Benefit Managers to extract unit cost savings from drug manufacturers for formulary coverage. Given certain states' current and potential ongoing fiscal crises, a growing number of states are considering a variety of cost- control strategies, including capitated managed care plans that typically contain cost by restricting access to certain treatments. There have also been multiple recent U. S. congressional inquiries and proposed and adopted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs and biologics. In addition, Congress and multiple presidential administrations have indicated that they will continue to seek new legislative and / or administrative measures to control drug costs. These initiatives recently culminated in the enactment of the Inflation Reduction Act, or the IRA, in August 2022, which will, among other things, allows 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 seven 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 2023 and 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. We anticipate that additional state and federal healthcare measures could be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for cytisinicline, or additional pricing pressures. Anti- Corruption. The Foreign Corrupt Practices Act of 1977, as amended, or FCPA, prohibits U. S. corporations and their representatives from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Other countries have enacted similar anti- corruption laws and / or regulations. Individual states, acting through their attorneys general, have sought to regulate the marketing of prescription drugs under state consumer protection and false advertising laws. Outside the United States We expect to encounter similar regulatory and legislative issues in most other countries in which we seek to develop and commercialize cytisinicline. New Drug Approvals and Pharmacovigilance. In the EU, the approval of new drugs may be achieved using the Mutual Recognition Procedure, the Decentralized Procedure or the EU Centralized Procedure. These procedures apply in the EU member states, plus the EEA countries, Norway, Iceland and Liechtenstein. The use of these procedures generally provides a more rapid and consistent approval process across the EU and EEA than was the case when the approval processes were operating independently within each country. In 2012, new pharmacovigilance legislation came into force in the EU. Key changes included the establishment of a new Pharmacovigilance Risk Assessment Committee within the EMA, with responsibility for reviewing and making recommendations on product safety issues for the EU authorities. It also introduced the possibility for regulators to require

pharmaceutical companies to conduct post- authorization efficacy studies at the time of approval, or at any time afterwards in light of scientific developments. There are also additional requirements regarding adverse drug reaction reporting and additional monitoring of products. Outside developed markets such as the EU and Japan, pharmacovigilance requirements vary and are typically less extensive. Health authorities in many middle- and lower- income countries require marketing approval by a recognized regulatory authority (i. e., similar to the authority of the FDA or the EMA) before they begin to conduct their application review process and / or issue their final approval. Many authorities also require local clinical data in the country' s population in order to receive final marketing approval. These requirements delay marketing authorization in those countries relative to the United States and Europe. CONTRACT RESEARCH AGREEMENTS Our strategy is to outsource certain product development activities and have established contract research agreements for, non- clinical, clinical, manufacturing and some data management services. We choose which business or institution to use for these services based on their expertise, capacity and reputation and the cost of the service. We also provide or have provided quantities of our product candidates to academic research institutions to investigate the mechanism of action ~~and evaluate novel combinations of product candidates with other cancer therapies in various cancer indications~~. These collaborations expand our research activities for our product candidates with modest contributions from us. MANUFACTURING We do not own or operate manufacturing facilities for the production of cytisinicline, though we may develop our own manufacturing operations in the future. We currently partner with Sopharma as supplier and contract manufacturer for our required raw materials, active pharmaceutical ingredients and finished drug product for our clinical trials. In addition to our Sopharma relationship, we utilize contract manufacturing organizations for the clinical packaging supplies of cytisinicline and are in the process of contracting with additional contract manufacturing organizations for commercial drug supply. We currently employ internal resources and third- party consultants to manage our clinical manufacturing activities. Sopharma sources cytisinicline from natural sources including trees and shrubs from the Faboideae subfamily of plant species. The seeds of cytisinicline containing plants are harvested annually, dried and processed into cytisinicline. The seeds in their natural state are highly toxic and the extraction process removes the toxins to produce highly purified cytisinicline. Sopharma controls a number of orchards throughout Bulgaria in addition to sourcing seeds and cytisinicline starting material from certain third- party suppliers. We expect to continue stockpiling cytisinicline to meet the projected demand ~~from us~~ upon commercial launch. The active pharmaceutical ingredient, or API, manufacturing process utilizes a series of techniques including solvent extraction, recrystallization, filtration, and purification. Critical control steps and manufacturing intermediates have been identified and are controlled by internally developed specifications and methods to ensure a consistent and reproducible process. The highly purified cytisinicline is dried, sieved and packed for storage until further processing into drug product. The cytisinicline API manufacturing process has been developed and refined over many years of manufacture by Sopharma, which has significant expertise in manufacturing cytisinicline. Sopharma manufactures cytisinicline API in its facilities in Bulgaria, which are near the capital, Sofia. The API processing facility complies with EU cGMP requirements and has been inspected by the Bulgarian Drug Agency. During 2022, Sopharma built a new API facility specifically for cytisinicline within its tableting plant in Sofia. **Sopharma currently does not have FDA approval of its facilities in Bulgaria.** Raw materials are essential to our business and are normally available in quantities adequate to meet the needs of our business. Where there are exceptions, the temporary unavailability of those raw materials has not historically had a material adverse effect on our financial results however, uncertainties in supply chain, transportation logistics and costs, and political and economic conditions could result in disruptions in our operations and materially impact our financial results. SALES AND MARKETING Our commercial strategy may include the use of strategic partners, distributors, a contract sale force or the establishment of our own commercial marketing and sales infrastructure. We plan to further evaluate these alternatives including the potential to market and distribute directly to consumers via traditional and virtual channels. We intend to seek commercial partnerships in ex- U. S. territories. INTELLECTUAL PROPERTY The U. S. Supreme Court has held that certain claims to naturally occurring substances are not patentable. Cytisinicline is a naturally occurring product and, therefore, the compound itself is not patentable in the United States. Furthermore, cytisinicline has been used in other parts of the world for decades, creating further challenges to patenting uses of the compound. Our development and commercialization of cytisinicline is protected by our exclusive supply agreement with Sopharma and Sopharma' s proprietary technology, experience and expertise in cytisinicline extraction. In addition, we intend to utilize market exclusivity laws including those under the Hatch- Waxman Act in the United States and exclusivity under Directive 2004 / 27 / EC in the EU. Additionally, we are actively building an intellectual property portfolio around our clinical- stage product candidate and research programs. A key component of this portfolio strategy is to seek international patent protection with patent applications in the United States and in major market countries that we consider important to the development of our business. As of December 31, ~~2023~~ **2024**, we ~~own~~ **control** a portfolio of ~~four~~ patent families **that are owned, co- owned and in- licensed**. Those families cover cytisinicline **dosing methods, cytisinicline** derivatives ~~(being prosecuted~~ **, cytisinicline salts, methods of cytisinicline extraction, and cytisinicline formulations, among other inventions,** in the United States ~~, Australia, Canada, China, Europe, U. K.~~ and ~~Japan)~~ **foreign jurisdictions. As of December 31**, **2024** ~~novel cytisinicline salts (being prosecuted in the United States~~, ~~Australia~~ **we owned**, **co- owned or in- licensed over 20** ~~Canada, China, Europe, Hong Kong, South Korea, Japan and New Zealand with~~ issued patents ~~in the U. K., Canada, United States, Mexico~~ and **over** ~~South Africa), and novel cytisinicline dosing methods being prosecuted in the United States, Brazil, Canada, China, Europe, Japan, South Korea, Mexico, and New Zealand, with issued patents in the United States. Additionally, we have in- licensed rights from Sopharma to two patent families relating to a new method of cytisinicline extraction, as well as cytisinicline formulations and one family from a third party relating to cytisine purity. As of December 31, 2023, we owned or in- licensed 26 issued patents and~~ 50 pending patent applications. These patents **and applications, if granted,** have ~~expirations~~ **expiration** dates ranging from 2037 to 2042, absent any term adjustments or extensions. Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates and other discoveries, inventions, trade secrets and know- how that are critical to our business operations. Our success also

depends in part on our ability to operate without infringing the proprietary rights of others, and in part, on our ability to prevent others from infringing our proprietary rights. A comprehensive discussion on risks relating to intellectual property is provided under " Risk Factors — Risks Related to Our Intellectual Property. " In addition to patent protection, we rely on trade secrets, trademark protection and know- how to expand our proprietary position around our chemistry, technology and other discoveries and inventions that we consider important to our business. We also seek to protect our intellectual property in part by entering into confidentiality agreements with our employees, consultants, scientific advisors, clinical investigators and other contractors and also by requiring our employees, commercial contractors and certain consultants and investigators, to enter into invention assignment agreements that grant us ownership of any discoveries or inventions made by them. COMPETITION The development and commercialization of new products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to smoking cessation and other product candidates that they may seek to develop or commercialize in the future. We are aware that many companies have therapeutics marketed or in development for smoking cessation. We expect that our competitors and potential competitors have historically dedicated, and will continue to dedicate, significant resources to aggressively develop and commercialize their products in order to take advantage of the significant market opportunity. Prescription and Over- the- Counter Treatments Only two non- nicotine, prescription treatments for smoking cessation are currently available in the United States; " varenicline " (formerly marketed by Pfizer as Chantix) and " bupropion " (formerly marketed by GlaxoSmithKline as Zyban). Both are currently available as generic formulations. Varenicline requires a three- month treatment period and bupropion is recommended for a period between seven and 12 weeks. While both have been proven effective in aiding smoking cessation, they are also associated with significant side effects and early discontinuations from treatment. Varenicline' s labeling indicates elevated instances of nausea, abnormal dreams, constipation, flatulence, and vomiting may be experienced by varenicline- treated patients compared to placebo- treated patients, and bupropion' s product label discloses potential adverse reactions including insomnia, rhinitis, dry mouth, dizziness, nervous disturbance, anxiety, nausea, constipation, arthralgia and seizures. Both varenicline and buproprion have warning and precautions for neuropsychiatric adverse events, including suicidal ideations. High uptake into the brain combined with activity at " off target " receptors could be responsible for varenicline' s adverse event profile. The most common OTC treatments bought in pharmacies for smoking cessation in the United States and worldwide are NRTs such as nicotine gums, nicotine lozenges, and nicotine patches. Each of these products delivers nicotine to the body although they generally do so at different rates and to different parts of the body than does a traditional cigarette. As concluded by the authors of several published clinical trials conducted by others, these therapies are generally less effective than prescription treatments. Recognized brands include Niquitin, Nicotinell, Nicorette and Nicoderm. Depending on the duration of treatment, the average cost of certain OTC smoking cessation treatments can exceed prescription treatments. Pharmaceutical companies, including larger companies in the industry, who have extensive expertise in non- clinical and clinical testing and in obtaining regulatory approvals for products, may develop other OTC treatments for smoking cessation. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. HUMAN CAPITAL RESOURCES As of December 31, ~~2023~~ **2024** , we had a total of ~~22~~ **25** employees, of whom ~~thirteen~~ **fourteen** were engaged in research and development functions, including clinical development, regulatory affairs and manufacturing, and ~~nine~~ **eleven** were engaged in general and administrative functions, including accounting and finance, administration, and commercial. All of our employees have entered into non- disclosure agreements regarding our intellectual property, trade secrets and other confidential information. None of our employees are represented by a labor union or covered by a collective bargaining agreement, nor have we experienced any work stoppages. We believe that we maintain satisfactory relations with our employees. From time to time, we also use outside consultants to provide advice on our clinical development plans, research programs, administration and potential acquisitions of new technologies. We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We emphasize a number of measures and objectives in managing our human capital assets, including, among others, employee engagement, development, and training, talent acquisition and retention, **and** employee safety and wellness ~~, diversity and inclusion, and compensation and pay equity~~ . We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well- being across all aspects of their lives, including health care, retirement planning and paid time off. COMPANY INFORMATION We were incorporated in California in October 1991 and subsequently reorganized as a Delaware corporation in March 1995. Our principal executive ~~office~~ **offices** ~~is~~ **are** located at **22722 29th Dr. SE Suite 100 Bothell, WA 98021 and** 1040 West Georgia Street, Suite 1030, Vancouver, B. C. V6E 4H1, Canada and our telephone number is (604) 210- 2217. AVAILABLE INFORMATION We maintain a website at http: / / www. achievelifesciences. com. The information contained on or accessible through our website is not part of this Annual Report on Form 10- K. Our Annual Report on Form 10- K, Quarterly Reports on Form 10- Q, Current Reports on Form 8- K and amendments to reports filed or furnished pursuant to Sections 13 (a) and 15 (d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after we electronically file such reports with, or furnish those reports to, the SEC. The SEC also maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at http: / / www. sec. gov. ITEM 1A. RISK FACTORS Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10- K and in the other periodic and current reports and other documents we file with the Securities and Exchange Commission, before deciding to invest in our common stock. If any of the following risks materialize, our business, financial condition, results of operation and future prospects will likely be materially and adversely affected. In that

event, the market price of our common stock could decline, and you could lose all or part of your investment. This list is not exhaustive, and the order of presentation does not reflect management' s determination of priority or likelihood. Risks Related to Our Financial Condition and Capital Requirements ~~If we fail~~ **Substantial doubt exists as to our ability to continue as a going concern. Our ability to continue as a going concern is subject to material uncertainty and dependent on our ability** to obtain additional financing ~~when needed,~~ **. There is no assurance that** we **will obtain financing from** ~~may be unable to complete the~~ **other sources** ~~development, regulatory approval and commercialization of our product candidate~~ . **The uncertainty** ~~We have expended and continue to expend substantial funds in connection~~ with **respect to** our **operations** ~~product development activities~~ and ~~clinical trials and regulatory approvals~~ **the capital markets generally may make it more challenging to raise additional capital on favorable terms, if at all** . In addition, we expect to incur significant expenses and increasing operating losses for at least the next several years as we continue our clinical development of, seek regulatory approval for, and commercialize, cytisinicline and add personnel necessary to operate as a commercial- stage public company. We expect that our operating losses will fluctuate significantly from quarter to quarter and year to year due to timing of clinical development programs, efforts to achieve regulatory approval and ~~prepare for~~ commercialization. ~~Funds generated from~~ **Our current resources are insufficient to fund** our **planned** operations **for the next 12 months** ~~will be insufficient to enable us to bring all of our products currently under development to commercialization~~ . We will continue to require substantial additional capital to continue our clinical development activities and expand our regulatory, manufacturing and commercialization activities. Accordingly, we will need to raise substantial additional capital ~~to continue to fund our operations~~ from the sale of our securities, debt, partnering arrangements, non- dilutive fundraising or other financing transactions in order to **continue to fund our operations and** finance the remaining development and commercialization of our product candidate **. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our clinical development, regulatory review and commercialization efforts** . The current financing environment in the United States, particularly for biotechnology companies like us, is challenging and we can provide no assurances as to when this will improve. Our business may be impacted by macroeconomic conditions, including **fluctuating** inflation, interest **and tariff** rates and market conditions as well as political events, war, terrorism, business interruptions and other geopolitical events and uncertainties beyond our control. These factors may make it challenging to raise additional capital on favorable terms, if at all. A severe or prolonged economic downturn could result in a variety of risks to our business, including in our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy also could strain our suppliers, possibly resulting in supply disruption. In addition, current macroeconomic conditions have caused ~~turmoil~~ **uncertainty** in **various** ~~the banking sector~~ **sectors** ~~. Further~~ , **including capital markets** ~~the maturity date of our Convertible Term Loan could accelerate in certain circumstances related to the timing of our submission and the FDA' s acceptance of a New Drug Application, or NDA~~ . For these reasons, among others, we cannot be certain that additional financing will be available when and as needed or, if available, that it will be available on acceptable terms. If financing is available, it may be on terms that adversely affect the interests of our existing stockholders. If adequate financing is not available, we may need to ~~continue to~~ reduce or eliminate our expenditures for research and development of cytisinicline, and may be required to suspend development of cytisinicline. Our actual capital requirements will depend on numerous factors, including: • the progress and results of our research and development programs; • the repayment or conversion of our outstanding debt; • ~~our commercialization activities and arrangements; •~~ the time and cost involved in obtaining regulatory approvals for our product candidate **; • our commercialization activities and arrangements** ; • the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights with respect to our intellectual property; • the effect of competing technological and market developments; • the effect of changes and developments in our existing collaborative, licensing and other relationships; • the effect of interest rate adjustments, which may impact the cost of our borrowing under our loan facility, which includes an adjustable- rate component; and • the terms of any new collaborative, licensing, commercialization and other arrangements that we may establish. We may not be able to secure sufficient financing on acceptable terms, or at all. Without additional funds, we may be forced to delay, scale back or eliminate some of our research and development activities or other operations and potentially delay product development in an effort to provide sufficient funds to continue our operations. If any of these events occur, our ability to achieve our development and commercialization goals would be adversely affected. As of December 31, ~~2023~~ **2024** , the principal amounts due under our debt instruments (including the **New** Debt Agreement, as **defined and** further described under the section entitled " Management' s Discussion and Analysis of Financial Condition and Results of Operations ") totaled $ ~~17~~ **10** . ~~3~~ **0** million. Servicing our debt requires a significant amount of cash. Our debt is subject to floating interest rates set in relation to the prime rate. Increases in interest rates have made and may continue to make our debt service costs increase. The **New** Convertible Term Loan **(as defined and further described under the section entitled " Management' s Discussion and Analysis of Financial Condition and Results of Operations ")** matures on December ~~22, 2024, but the Debt Agreement contains maturity acceleration clauses. In the event we fail to receive a Filing Communication that the FDA has accepted for filing our NDA with respect to cytisinicline for a smoking cessation indication, on or prior to July 31, 2024, the maturity date shall be August~~ 1, ~~2024~~ **2027** ~~or in the event we receive a Filing Communication with respect to cytisinicline for a smoking cessation indication on or prior to August 14~~ , **subject** ~~2024, but where such Filing Communication specifies any material deficiencies or material filing review issues with respect~~ to **certain potential** ~~such NDA, the maturity date shall be August 15, 2024; provided, further, that in the event we have submitted the NDA on or prior to June 30, 2024, each of the maturity dates listed above shall be extended by one calendar month. In light of our recent discussions with the FDA and our current plans for the submission of an NDA for cytisinicline, if we are unable to secure a waiver or renegotiate the terms of the Debt Agreement, we expect that the Convertible Term Loan will mature on August 1, 2024. If we are at any time unable to service our indebtedness, we may be required to attempt to renegotiate the terms of the loan, seek to refinance all or a portion of the loan or seek additional financing. We and the Lenders have entered into a non- binding Term Sheet for an~~

~~extension~~ **extensions** ~~of the maturity date for the Convertible Term Loan, but there is no guarantee that we will be able to enter into a definitive agreement with the Lenders on these terms or any at all~~. We currently do not generate any cash flow from operations and if we are unable to make interest and / or principal payments when due, we would be in default under the **New** Debt Agreement. We may be required to raise additional capital through future financings or sales of assets to enable us to make interest payments and / or repay our outstanding indebtedness as it becomes due. There can be no assurance that we will be able to generate cash or raise additional capital. Any debt financing that is available could cause us to incur substantial costs and subject us to covenants that significantly restrict our ability to conduct our business. If we seek to complete additional equity financings, the interests of existing stockholders may be diluted. If we are unable to service our loan, the lender may foreclose on and sell the assets securing such indebtedness to satisfy our payment obligations, which could prevent us from accessing those assets for our business and conducting our business as planned, which could materially harm our financial condition and results of operations. Our obligations under the **New** Debt Agreement are secured by substantially all of our assets, other than intellectual property. If we are unable to make payment on our secured debt instruments when due, the lender under such instrument may foreclose on and sell the assets securing such indebtedness to satisfy our payment obligations, which could prevent us from accessing those assets for our business and conducting our business as planned, which could materially harm our financial condition and results of operations. Further, if we are liquidated, the rights of the ~~Lenders~~ **Lender** to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. The ~~Lenders~~ **Lender** could declare a default under the **New** Debt Agreement upon the occurrence of any event that the ~~Lenders~~ **Lender** ~~interpret~~ **interprets** as a material adverse change as defined under the **New** Debt Agreement, thereby requiring us to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by the ~~Lenders~~ **Lender** of an event of default could significantly harm our business, financial condition, results of operations and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility. Further, the **New** Debt Agreement contains customary affirmative and restrictive covenants, including covenants regarding the incurrence of additional indebtedness or liens, investments, transactions with affiliates, delivery of financial statements, payment of taxes, maintenance of insurance, dispositions of property, mergers or acquisitions, and the requirement we keep substantially all of our cash and investments with SVB, among other customary covenants. We are also restricted from paying dividends or making other distributions or payments on capital stock, subject to limited exceptions. The ~~Loan~~ **New Debt** Agreement includes customary representations and warranties, events of default and termination provisions. Our existing and any future indebtedness may limit our cash resources available to invest in the ongoing needs of our business ~~.~~ Our outstanding debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including: • reducing cash resources available to fund working capital, capital expenditures, product development efforts and other general corporate purposes; • increasing our vulnerability to adverse changes in general economic, industry and market conditions; • subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing; • limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and • placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options. We intend to satisfy our current and future debt service obligations with our existing cash and funds from external sources. Nonetheless, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing or any future debt facility. Funds from external sources may not be available on acceptable terms, if at all. We have incurred losses since inception, have a limited operating history on which to assess our business and anticipate that we will continue to incur losses for the foreseeable future. We are a **late** ~~clinical development~~ stage **clinical** specialty pharmaceutical company with a limited operating history, are not profitable, have incurred losses in each year since our inception and expect to continue incurring losses for the foreseeable future. Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to developing our cytisinicline product candidate and supporting our operations. To date, we have funded the company primarily through the sale of equity securities and convertible promissory notes. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We further expect that our expenses will increase substantially if and as we: • continue the clinical development of cytisinicline; • **establish a sales** ~~advance cytisinicline development into larger~~, **marketing** ~~more expensive clinical trials; • initiate additional non- clinical~~, **and distribution infrastructure to commercialize** ~~clinical, or other trials or studies for~~ cytisinicline; • seek to attract and retain skilled personnel; • undertake the manufacturing of cytisinicline or increase volumes manufactured by third parties; • seek regulatory approvals and reimbursement for cytisinicline; • **experience delays in the development of our cytisinicline candidate, including delays in clinical trials and delays in regulatory review; • initiate additional non-clinical, clinical, or other trials or studies for cytisinicline; •** make milestone, royalty or other payments under third- party license and / or supply agreements; • ~~establish a sales, marketing, and distribution infrastructure to commercialize any product for which we may obtain marketing approval and market for ourselves; • seek to discover, identify, assess, acquire, and / or develop other product candidates; •~~ seek to establish, maintain, protect, and expand our intellectual property portfolio; • ~~experience delays in the development of~~ **seek to discover, identify, assess, acquire, and /** ~~our~~ **or** ~~cytisinicline~~ **develop other product** ~~candidate~~ **candidates** ~~, including delays in clinical trials~~; • encounter safety concerns; or • require additional studies to support regulatory approval and commercialization. Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. We have never generated any revenue from product sales and may never be profitable. We have no products approved for commercialization and have never generated any revenue from product sales. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize cytisinicline. We do not anticipate generating

revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to: • completing research and development of cytisinicline; • obtaining regulatory approvals for cytisinicline; • manufacturing product and establishing and maintaining supply and manufacturing relationships with third parties that are commercially feasible, satisfy regulatory requirements and meet our supply needs in sufficient quantities to satisfy market demand for cytisinicline, if approved; • marketing, launching and commercializing any product for which we obtain regulatory approval, either directly or with a collaborator or distributor; • obtaining reimbursement or pricing for cytisinicline that supports profitability; • gaining market acceptance of cytisinicline as a treatment option; • addressing any competing or alternative products, including the potential for generic cytisinicline products; • protecting and enforcing our intellectual property rights, if any, including patents, trade secrets, and know- how; • negotiating favorable terms in any collaboration, licensing, commercialization, or other arrangements into which we may enter; and • attracting, hiring, and retaining qualified personnel. Even if a product candidate that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing that candidate. Additionally, if we are not able to generate sufficient revenue from the sale of any approved products to cover our operating costs, we may never become profitable. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidate may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement from third- party payors, and adequate market share for our product candidate in those markets. 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 with Silicon Valley Bank, or SVB, both in the United States and internationally, 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. Under the terms of the **New** Debt Agreement, we are required to keep substantially all of our cash and investments with SVB. In March 2023, SVB was closed by the California Department of Financial Protection and Innovation, which also appointed the FDIC as receiver. Within days, the FDIC assisted depositors of the bank access funds and we were able to regain full access to our cash and cash equivalents with SVB. In May 2023, First Citizens assumed all of SVB' s deposits and loans. While our deposits are backed by the FDIC, that support may not last or be honored in the future and we could be materially impacted. Risks Related to the Development of Our Product Candidate Cytisinicline We are currently dependent on the potential development of a single product candidate, cytisinicline. We are still developing cytisinicline and it cannot be marketed or sold in the United States or in foreign markets until regulatory approval has been obtained from the FDA or applicable foreign regulatory agencies. The process of obtaining regulatory approval is expensive and time consuming. The FDA and foreign regulatory authorities may never approve cytisinicline for sale and marketing, and even if cytisinicline is ultimately approved, regulatory approval may be delayed or limited in the United States or in other jurisdictions. Even if we are authorized to sell and market cytisinicline in one or more markets, there can be no assurance that we will be able to successfully market cytisinicline or that cytisinicline will achieve market acceptance sufficient to generate profits. If we are unable to successfully develop and commercialize cytisinicline due to failure to obtain regulatory approval for cytisinicline, to successfully market cytisinicline, to generate profits from the sale of cytisinicline, or due to other risk factors outlined in this report, it would have material adverse effects on our business, financial condition. **We are dependent upon a single company for the manufacture and supply of cytisinicline.** Our single product candidate, cytisinicline, has been in- licensed from a third party, Sopharma **AD, or** ~~. We are required to continue to contract with~~ Sopharma, **a Bulgarian third- party supplier.** ~~to continue our development of, and potential commercialization of, cytisinicline pursuant~~ **Pursuant** to a supply agreement with **Sopharma, Sopharma is currently the exclusive supplier of cytisinicline and cytisinicline active pharmaceutical ingredients (API). We plan to engage other third parties for our manufacturing process, including, if cytisinicline is approved, to manufacture cytisinicline on a commercial scale, with tableting, blistering and packaging. Our current supply agreement with Sopharma expires on July 28, 2037, unless extended by agreement between us and** Sopharma. Sopharma currently manufactures all of its cytisinicline API in its facilities in Bulgaria. The conflict in Ukraine, including the possibility of expanded regional or global conflict and related economic sanctions, may have negative impacts on Sopharma' s business, which could cause them to reduce or terminate investments in the cytisinicline program. If the supply agreement with Sopharma is terminated **or if Sopharma is otherwise unable to meet its obligations under the supply agreement** , we will need to secure alternative supply and manufacturing capabilities for cytisinicline **and / or cytisinicline API** , which we may not be able to do on commercially viable terms or at all and would likely delay development, regulatory approval and commercialization. **The therapeutic component of** our product candidate,cytisinicline,is derived from the seeds of trees and shrubs from the Faboideae subfamily of plant species,which grow in the mountains of Southern Europe and other limited locations around the world.We have and will continue to pursue alternative sources for cytisinicline,including synthetic routes,however,all of the cytisinicline sourced to date for our product candidate has been from natural sources and there is no guarantee that any potential synthetic route developed will be commercially viable.We currently secure cytisinicline exclusively from Sopharma ~~,a Bulgarian third- party supplier.Our current supply agreement with Sopharma expires on July 28,2037,unless extended by mutual agreement of us and Sopharma~~ .There can be no assurances that trees and shrubs from the Faboideae subfamily of plant species will continue to grow in sufficient quantities around the world to **meet our forecasts or commercial supply requirements or that the countries from which we can secure them will continue to allow the exportation of cytisinicline.** We plan to submit an NDA to the FDA for **the marketing** approval of cytisinicline as ~~an aid~~ **a drug therapy** in treating nicotine dependence for smoking cessation, based largely on data from our ~~recently~~ completed Phase 3 ORCA- 2 and ORCA- 3 clinical trials and ~~planned~~ **the ongoing** ORCA- OL

trial; however, there can be no assurance that the data from our clinical trials will ultimately support an NDA filing or that the FDA will grant marketing approval of cytisinicline without additional clinical or nonclinical studies, or at all. Drug product candidates must demonstrate substantial evidence of effectiveness, as well as safety to be approved in the United States. The FDA has interpreted that statutory standard as generally requiring at least two adequate and well- controlled clinical trials, each convincing on its own, to establish effectiveness and a safety profile. Under certain circumstances the FDA will determine that data from one adequate and well- controlled clinical trial together with confirmatory evidence obtained prior to or after such clinical trial are sufficient to constitute substantial evidence of effectiveness. Cytisinicline is a naturally occurring, plant- based alkaloid. Cytisinicline is structurally similar to nicotine and has a well- defined, dual- acting mechanism of action that is both agonistic and antagonistic. It is believed to aid in smoking cessation and the treatment of nicotine ~~addiction~~ **dependence** by interacting with nicotine receptors in the brain, reducing the severity of nicotine withdrawal symptoms through agonistic effects on nicotine receptors and reducing the reward and satisfaction associated with nicotine through antagonistic properties. Cytisinicline has been studied in two company- sponsored randomized, multicenter, double- blind, placebo **-** controlled Phase 3 clinical studies that randomized a total of 1, 602 adult smokers in 37 study sites across the United States. The FDA has advised us that long- term exposure data to assess for safety beyond 12 weeks will be needed to adequately assess safety risks given that the FDA views smoking cessation drugs as products for chronic, repeated, and intermittent use as patients may relapse and require subsequent courses of treatment over a lifetime. In the first quarter of 2024, we reached agreement with the FDA that a single, open- label study, which we refer to as ORCA- OL, evaluating the long- term safety effects of cytisinicline will be sufficient to complete the requirement and enable an NDA submission. **We initiated the ORCA- OL trial in May 2024 and in October 2024 we announced the completion of enrollment of 479 subjects. In January 2025, we announced that the ORCA- OL trial had reached the goal of at least 300 subjects completing six months of cumulative cytisinicline exposure.** However, regardless of these discussions and the results of the ORCA- OL open label study, the FDA may determine that: • the existing data, and the data from the ORCA- OL open label study, may not be sufficient and the FDA may require additional clinical and / or nonclinical studies prior to filing an NDA ~~and~~ **or prior to** approval of cytisinicline for treating nicotine dependence for smoking cessation in adults; • 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 product candidate' s risk- benefit **assessments** ~~ratios for the proposed indication~~ may not be acceptable **for the proposed indication** ; • the data collected from clinical trials of our product candidate may not be sufficient to support the submission of an application for marketing authorization; and • third- parties' manufacturing processes or facilities with which we contract for clinical and commercial supplies may not meet the standards required for approval. Failure to obtain regulatory approval to market our product candidate would significantly harm our business, results of operations, and prospects . The therapeutic component of our product..... and our business will be adversely affected . Results of earlier clinical trials of cytisinicline are not necessarily predictive of future results, and any advances of cytisinicline into clinical trials may not have favorable results or receive regulatory approval. Even if our clinical trials are completed as planned, we cannot be certain that their results will be consistent with the results of the earlier clinical trials of cytisinicline. Positive results in non- clinical testing and past clinical trials with respect to the safety and efficacy of cytisinicline do not ensure that results from subsequent clinical trials will also be positive, and we cannot be sure that the results of subsequent clinical trials will replicate the results of prior clinical trials and non- clinical testing. Any such failure may cause us to abandon cytisinicline, which would negatively affect our ability to generate any product revenues. Clinical trials, including the ~~planned~~ **ongoing** ORCA- OL trial, are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities. Any advances of cytisinicline into clinical trials may not have favorable results or receive regulatory approval. Clinical development is expensive, time consuming and involves significant risk. We cannot guarantee that any clinical trial, including the ~~planned~~ **ongoing** ORCA- OL trial, will be conducted as planned or completed on schedule, if at all. Events that may prevent successful or timely completion of the ~~planned~~ **ongoing** ORCA- OL trial, but are not limited to: ~~• delays in recruiting qualified subjects who previously participated in the ORCA- program studies;~~ • subjects terminating enrollment in the ORCA- OL trial; • failure by clinical sites, CROs or other third parties to adhere to clinical trial requirements; • failure by clinical sites, CROs or other third parties to perform in accordance with the good clinical practices requirements of the FDA or applicable foreign regulatory guidelines; • disruptions to our supply chain for the cytisinicline required for the ORCA- OL trial; • the occurrence of previously unknown on unobserved adverse events or tolerability issues associated with our product candidate, including those significant enough to stop the trial or for the FDA or other regulatory agencies to put the ORCA- OL trial on hold; • the cost of the ORCA- OL trial; • negative or inconclusive results from the ORCA- OL trial, which may result in us deciding, or regulators requiring us, to conduct further additional clinical trials or abandon development programs in ongoing or other planned indications for cytisinicline; • discovery of impurities in our cytisinicline drug product, such as nitrosamines, above the regulators' prescribed thresholds; and • delays in the manufacture or packaging of sufficient quantities of cytisinicline for use the ORCA- OL trial. Any inability to successfully complete clinical development and obtain regulatory approval for cytisinicline could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to cytisinicline, we may need to conduct additional non- clinical trials, or the results obtained from such new formulation may not be consistent with previous results obtained. Clinical trial delays could result in delayed regulatory approval and potential commercialization, as well as shorten any periods during which our products have patent protection and may allow competitors to develop and bring products to market before we do, which could impair our ability to successfully commercialize cytisinicline and may harm our business and results of operations. Further, even if the ORCA- OL trial is completed as planned, we cannot be certain that its long- term safety results will be consistent with the results of the earlier clinical trials of cytisinicline or support an NDA filing. Positive results in non- clinical testing and past clinical trials with respect to the adequate safety and efficacy of cytisinicline do not ensure that results from subsequent clinical trials will also be positive or adequate, and we cannot be sure that the results of

subsequent clinical trials will replicate the results of prior clinical trials and non- clinical testing. Any such failure may cause us to abandon cytisinicline, which would negatively affect our ability to conduct our business and generate any product revenues and result in a loss of company value. Undesirable side effects caused by cytisinicline could cause us or regulatory authorities to interrupt, delay, or terminate clinical trials. Even if approved, these could result in a restrictive label, a shelf life that is not commercially viable or delay regulatory approval by the FDA or comparable foreign authorities. If contaminants, or impurities such as nitrosamines, are discovered in quantities above regulators' thresholds within our supply of cytisinicline, we may potentially delay product development and approval or have a material adverse impact on our business. Failure to reach agreement with the FDA on acceptable intake levels for impurities, such as nitrosamines, or exceeding agreed upon levels could delay or prevent regulatory approval. Additionally, even if cytisinicline receives marketing approval and we or others later identify undesirable side effects caused by cytisinicline, potentially significant negative consequences could result, including but not limited to: • regulatory authorities may withdraw approvals of cytisinicline; • regulatory authorities may require additional warnings on the cytisinicline label; • we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and / or other elements to assure safe use; • we could be subject to product liability claims for harm caused to patients; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of cytisinicline, even if approved, and could significantly harm our business, results of operations, and prospects . Our product development program may not uncover all possible adverse events that patients who take cytisinicline or our other product candidates may experience. The number of subjects exposed to cytisinicline or our other product candidates and the average exposure time in the clinical development program may be inadequate to detect rare adverse events, or chance findings, that may only be detected once the product is administered to more patients and for greater periods of time. Clinical trials by their nature utilize a sample of the potential patient population. We cannot be fully assured that any and all rare and severe side effects of cytisinicline will be uncovered. Such rare and severe side effects may only be uncovered with a significantly larger number of patients exposed to cytisinicline or over a significantly longer period of time. If such safety problems occur or are identified after cytisinicline reaches the market in the United States, or if such safety problems occur or are identified in foreign markets where cytisinicline is currently marketed, the FDA may require that we amend the labeling of cytisinicline or recall it, or may even withdraw approval for cytisinicline. If the use or misuse of cytisinicline harms patients, or is perceived to harm patients even when such harm is unrelated to cytisinicline, our regulatory approvals, if any, could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. If we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, a material liability claim could adversely affect our financial condition. The use or misuse of cytisinicline in clinical trials and the sale of cytisinicline if marketing approval is obtained, exposes us to the risk of potential product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product. There is a risk that cytisinicline may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, during the course of treatment, patients may suffer adverse events for reasons that may be related to cytisinicline. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market cytisinicline, if any, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which an adverse event is unrelated to cytisinicline, an investigation into such circumstance may be time- consuming or inconclusive. Such investigations may delay our regulatory approval process or impact and limit the type of regulatory approvals cytisinicline receives or maintains. As a result, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations and reputation. If we obtain marketing approval for cytisinicline, we will need to expand our insurance coverage to include the sale of commercial products. We cannot know if we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it in sufficient amounts to protect us against losses due to liability, on acceptable terms, or at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is a risk that these third parties could incur liability and bring a claim under such indemnities. An individual may also bring a product liability claim against us alleging that cytisinicline causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. 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. Any product liability claim brought against us, with or without merit, could result in: • withdrawal of clinical trial volunteers, investigators, patients or trial sites or limitations on approved indications; • an inability to commercialize, or if commercialized, a decreased demand for, cytisinicline; • if commercialized, product recalls, withdrawals of labeling, marketing or promotional restrictions or the need for product modification; • initiation of investigations by regulators; • loss of revenue, if any; • substantial costs of litigation, including monetary awards to patients or other claimants; • liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves; • increased product liability insurance rates, or inability to maintain insurance coverage in the future on acceptable terms, if at all; • diversion of management' s attention from our business; and • damage to our reputation and the reputation of our products and our technology. Product liability claims may subject us to the foregoing and other risks, which could have a material adverse effect on our business, financial condition or results of operations. Our business may be negatively affected by weather conditions, natural disasters, and the availability of natural resources, as well as by climate change. In recent years, extreme weather events and changing weather patterns such as storms, flooding, drought, and temperature changes appear to have become more common. The production of cytisinicline from the Faboideae subfamily of plant species depends on the

availability of natural resources, including sufficient rainfall. ~~Our exclusive~~ **Sopharma, our** supplier of cytisinicline ~~, Sopharma~~ , could be adversely affected if it experiences a shortage of fresh water due to droughts or if it experiences other adverse weather conditions in the locations where cytisinicline is sourced. The long- term effects of climate change on general economic conditions and the pharmaceutical industry in particular are unclear and may heighten or intensify existing risk of natural disasters. As a result of such events, we could experience cytisinicline shortages ~~from Sopharma~~ , which could have a material adverse effect on our business, financial condition and results of operations. In addition, the manufacturing and other operations of Sopharma are located near earthquake fault lines in Sofia, Bulgaria. In the event of a major earthquake, we could experience business interruptions from the disruption of our cytisinicline supplies, which could have a material adverse effect on our business, financial condition and results of operations. We conduct clinical trials internationally, which may trigger additional risks. Conducting clinical trials in Europe or other countries outside of the United States has additional regulatory requirements that we have to meet in connection with our manufacturing, distribution, use of data and other matters. Failure to meet such regulatory requirements could delay our clinical trials, the approval, if any, of cytisinicline by the FDA or other regulatory authorities, or the commercialization of cytisinicline, or result in higher costs or deprive us of potential product revenues. For example, we have recently conducted clinical trials in Spain and Portugal and are subject to the local regulatory requirements of such jurisdictions. We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and human resources, we may forego or delay pursuit of opportunities with some programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or more profitable market opportunities. Our spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. We may also enter into additional strategic collaboration agreements to develop and commercialize some of our programs and potential product candidates in indications with potentially large commercial markets. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaborations, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement. Risks Related to Regulatory Approval of Cytisinicline and Other Legal Compliance Matters We will need approval from the FDA to commercialize cytisinicline in the United States and approvals from similar regulatory authorities in foreign jurisdictions to commercialize cytisinicline in those jurisdictions. In order to obtain FDA approval of cytisinicline, we must submit an NDA to the FDA, demonstrating that cytisinicline is safe, pure and potent, and effective for its intended use. This demonstration requires significant research including completion of clinical trials. Satisfaction of the FDA' s regulatory requirements typically takes many years, depending upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. We cannot predict whether our clinical trials will demonstrate the safety and efficacy of cytisinicline or if the results of any clinical trials will be sufficient to advance to the next phase of development or for approval from the FDA. We also cannot predict whether our research and clinical approaches will result in data that the FDA considers safe and effective for the proposed indications of cytisinicline. The FDA has substantial discretion in the product approval process. The approval process may be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our applications. We may never obtain regulatory approval for cytisinicline. Failure to obtain approval from the FDA or comparable regulatory authorities in foreign jurisdictions to commercialize cytisinicline will leave us without saleable products and therefore without any source of revenues. In addition, the FDA may require us to conduct additional clinical testing or to perform post- marketing studies, as a condition to granting marketing approval of a product or permit continued marketing, if previously approved. If conditional marketing approval is obtained, the results generated after approval could result in loss of marketing approval, changes in product labeling, and / or new or increased concerns about the side effects or efficacy of a product. The FDA has significant post- market authority, including the explicit authority to require post- market studies and clinical trials, labeling changes based on new safety information and compliance with FDA- approved risk evaluation and mitigation strategies. The FDA' s exercise of its authority has in some cases resulted, and in the future could result, in delays or increased costs during product development, clinical trials and regulatory review, increased costs to comply with additional post- approval regulatory requirements and potential restrictions on sales of approved products. In foreign jurisdictions, the regulatory approval processes generally include the same or similar risks as those associated with the FDA approval procedures described above. We cannot be certain that we will receive the approvals necessary to commercialize cytisinicline for sale either within or outside the United States. ~~Even if~~ **Further, in June 2024, the U. S. Supreme Court reversed its longstanding approach under the Chevron doctrine, which provided for judicial deference to regulatory agencies, including the FDA. As a result of this decision,** we ~~obtain~~ **cannot be sure whether there will be increased challenges to existing agency regulations or how lower courts will apply the decision in the context of other regulatory schemes without more specific guidance from the U. S. Supreme Court. For example, this decision may result in more companies bringing lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, which could undermine the FDA' s authority, lead to uncertainties in the industry, and disrupt the FDA' s normal operations, which could impact the timely review of any regulatory filings or applications we submit to the FDA. Disruptions at the FDA may slow the time necessary for new products to be reviewed and / or approved, which would adversely affect our business. In addition, there is substantial uncertainty regarding new initiatives and how these might impact the FDA, its implementation of laws, regulations, policies and guidance and its personnel. Similar initiatives may also be directed toward other**

government agencies. These initiatives could prevent, limit or delay development and regulatory approval **of our product candidates, which would adversely affect our business. Disruptions at the FDA may slow the time necessary for new products to be reviewed and /** ~~for -~~ **or** ~~cytisinicline~~ **approved , which would adversely affect our business. Changes in FDA staffing could result in delays in the FDA' s responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. If any legislation, executive orders, or lapses in agency funding impose constraints on the FDA' s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. Similar consequences would also result in the event of another significant shutdown of the federal government. For example, in 2024, the U. S. government was on the verge of a shutdown and has previously shut down several times, and certain regulatory agencies, such as the FDA, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, or if geopolitical or global health concerns prevent the FDA 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, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. FDA- regulated industries, such as ours, face uncertainty with regard to the regulatory environment** we will **face as we proceed** ~~remain subject to ongoing regulatory requirements in connection~~ with **research, development and commercialization. Some of** ~~the~~ **these** ~~sale and distribution~~ **efforts have manifested to date in the form** of **personnel measures that could impact** ~~cytisinicline. Even if cytisinicline is approved by~~ the FDA **' s ability** ~~or comparable foreign regulatory authorities, we will be subject~~ to **hire** ~~ongoing regulatory requirements with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing clinical trials,~~ and ~~submission of safety~~ **retain key personnel , which** ~~efficacy and other post- approval information, including both federal and state requirements in the United States and the requirements of comparable foreign regulatory authorities. Compliance with such regulatory requirements will likely be costly and the failure to comply would~~ **could** ~~likely~~ result in ~~penalties, up~~ **delays or limitations on our ability** to **obtain guidance** ~~and including, the loss of such approvals~~ from the FDA **on** ~~or~~ **our product candidates** ~~comparable foreign regulatory authorities. Manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current cGMP regulations and corresponding foreign regulatory manufacturing requirements. As such, we, Sopharma and other contract manufacturers, if any, will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made~~ in **development** ~~any NDA or marketing authorization application. If Sopharma or our other contract manufacturers fail to maintain cGMP compliance or fail inspections with the FDA~~ and **obtain** ~~other regulators, then~~ **the requisite** ~~our business could severely be harmed. Ongoing post- approval monitoring and clinical trial obligations may be costly to us and the failure to meet such obligations may result in the withdrawal of such approvals. Any~~ regulatory approvals **in** ~~that we receive for cytisinicline may be subject to limitations on~~ the **future** ~~approved indicated uses for which cytisinicline may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of cytisinicline . We will be required to report adverse~~ **There remains general uncertainty regarding future activities. New executive orders,** ~~reactions -~~ **regulations** ~~and production problems -~~, **policies** ~~if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing product safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. If our -~~ **or guidance** ~~original marketing approval for cytisinicline was obtained through an accelerated approval pathway, we~~ could be **issued** ~~required to conduct a successful post- marketing clinical trial in order to confirm the clinical benefit for -~~ **or promulgated that adversely affects us** ~~our -~~ **or creates a more challenging or costly environment to pursue the development of new therapeutic** products. **Alternatively, state governments may attempt** ~~An unsuccessful post- marketing clinical trial or failure~~ to ~~complete such a trial could result in~~ **address or react to changes at the federal level with changes to** ~~the~~ **their own** ~~withdrawal of marketing approval. If a~~ regulatory **frameworks in** ~~agency discovers previously unknown problems with~~ a **manner that is** ~~product, such as~~ adverse **to** ~~events of unanticipated severity or~~ **our operations** ~~frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market~~ . If we **become negatively impacted** ~~fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things: • issue warning letters; • impose civil or criminal penalties; • suspend or withdraw regulatory approval; • suspend any of our ongoing clinical trials; • refuse to approve pending applications or supplements to approved applications submitted~~ by **future** ~~us; • impose restrictions on our operations, including closing our contract manufacturers' facilities; or • require a product recall. Any government~~ **governmental orders** ~~investigation of alleged violations of law would be expected to require us to expend significant time and resources in response and could generate adverse publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and the value of us and our operating results would be adversely affected. We may be subject , directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. If we obtain FDA approval for cytisinicline and begin commercializing it in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti- Kickback Statute, the federal False Claims Act, and physician sunshine laws and** regulations ~~. These laws may impact~~ , **policies** ~~among other things, our -~~ **or** proposed sales, marketing, and education..... voluntary compliance guidelines and the relevant compliance guidance ~~promulgated by the federal government , or otherwise restrict payments that may be made to healthcare providers and other -~~ **there** ~~potential referral sources; state laws that require~~

~~product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities~~ could be ~~subject to challenge under~~ **a material adverse effect** ~~one~~ **on** or more of such laws. In..... any other governmental regulations that apply to us ~~, we may be subject to penalties, including civil~~ and ~~criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate~~ our business ~~and its results of operations~~. Healthcare legislative and executive reform measures may have a material adverse effect on our business, financial condition or results of operations. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Healthcare Reform Law was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the U. S. pharmaceutical industry. The Healthcare Reform Law, among other things, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted, or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of specified branded prescription products, and promotes a new Medicare Part D coverage gap discount program. There have also been multiple recent U. S. congressional inquiries and proposed and adopted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs and biologics. In addition, Congress and multiple presidential administrations have indicated that they will continue to seek new legislative and / or administrative measures to control drug costs. These initiatives recently culminated in the enactment of the Inflation Reduction Act, or 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, 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 2023, 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 U. S. Affordable Care Act, or ACA, marketplaces through plan year 2025. These provisions **took** ~~will take~~ effect progressively starting in 2023, although they may be subject to legal challenges. We anticipate that additional state and federal healthcare measures could be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for cytisinicline, or additional pricing pressures. Currently, ACA and other federal laws and rules require most health insurance plans in the U. S. to cover some level of tobacco cessation treatments, including smoking cessation counseling and medications. If these provisions are repealed, in whole or in part, our business, financial condition, or results of operations could be negatively affected. Our ability to obtain services, reimbursement or funding may be impacted by possible reductions in federal spending in the United States as well as globally. U. S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least $ 1. 2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts include aggregate reductions to Medicare payments to providers of up to two percent per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. The full impact on our business of these automatic cuts is uncertain. If government spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop. Any reductions in government spending in countries outside the United States may also impact us negatively, such as by limiting the functioning of international regulatory agencies in countries outside the United States or by eliminating programs on which we may rely. **Even if** ~~In July 2021,~~ we ~~announced~~ **obtain regulatory approval for cytisinicline, we will remain subject to ongoing regulatory requirements in connection with the sale and distribution of cytisinicline. Even if cytisinicline is approved by the FDA or comparable foreign regulatory authorities, we will be subject to ongoing regulatory requirements with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing clinical trials, and submission of safety, efficacy and other post- approval information, including both federal and state requirements in the United States and the requirements of comparable foreign regulatory authorities. Compliance with such regulatory requirements will likely be costly and the failure to comply would likely result in penalties, up to and including, the loss of such approvals from the FDA or comparable foreign regulatory authorities. Manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current cGMP regulations and corresponding foreign regulatory manufacturing requirements. As such, we, Sopharma**

and other contract manufacturers, if any, will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or marketing authorization application. Sopharma currently does not have FDA approval of its facilities in Bulgaria. If Sopharma or our other contract manufacturers fail to maintain cGMP compliance or fail inspections with the FDA and other regulators, then our business could severely be harmed. Ongoing post- approval monitoring and clinical trial obligations may be costly to us and the failure to meet such obligations may result in the withdrawal of such approvals. Any regulatory approvals that we **receive for** ~~were awarded a grant from NIDA to evaluate the use of~~ cytisinicline ~~as a treatment~~ **may be subject to limitations on the approved indicated uses for which cytisinicline may be marketed** ~~for~~ - **or** ~~cessation~~ **to the conditions** of ~~nicotine c~~ **approval, or contain requirements for potentially costly post** - **marketing testing** ~~cigarette use. This initial grant award~~ , **including Phase 4 clinical trials** ~~in the amount of $ 320~~ , ~~000, commenced on August 1, 2021,~~ and **surveillance to monitor the safety and efficacy of cytisinicline. We will be required to report adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing product safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. If our original marketing approval for cytisinicline** was ~~utilized~~ **obtained through an accelerated approval pathway, we could be required to conduct a successful post- marketing clinical trial in order to confirm the clinical benefit for our products. An unsuccessful post-marketing clinical trial or failure** to complete ~~critical~~ **such a trial could result in the withdrawal of marketing approval. If a** regulatory ~~and clinical operational activities~~ **agency discovers previously unknown problems with a product** , such as ~~protocol finalization~~ **adverse events of unanticipated severity or frequency** , **or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things: • issue warning letters; • impose civil or criminal penalties; • suspend or withdraw regulatory approval; • suspend any of our ongoing** clinical ~~trial~~ **trials** ~~site identification~~ **; • refuse to approve pending applications or supplements to approved applications submitted by us; • impose restrictions on our operations** , ~~and submission~~ **including closing our contract manufacturers' facilities; or • require a product recall. Any government investigation** of **alleged violations of law would be expected to require us to expend significant time** ~~an~~ **and** ~~IND~~ **resources in response and could generate adverse publicity. Any failure** to **comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and** the **value of us and our operating results would be adversely affected. We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. If we obtain** FDA **approval** for ~~investigating~~ cytisinicline ~~in nicotine e- cigarette users. In November 2021, we announced that the FDA had completed their review~~ and **begin commercializing it** ~~accepted the IND to investigate cytisinicline as a cessation treatment in this population. In June 2022, following NIDA / NIH review of completed milestones, we announced that we were awarded the next grant funding from NIDA in the amount of approximately $ 2. 5 million to conduct the ORCA- V1 Phase 2 clinical study evaluating cytisinicline in 160 adult nicotine e- cigarette users~~ in the United States **, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti- Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business** . The **laws that may affect our ability to operate include: •** ~~full grant award of $ 2. 8 million covered approximately half of~~ the ~~ORCA~~ **federal Anti** - ~~V1 -~~ Kickback Statute,which prohibits,among other things,persons from knowingly and willfully soliciting,receiving,offering or paying remuneration,directly or indirectly,to induce,or in return for,the purchase or recommendation of an item or service reimbursable under a federal healthcare 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 from Medicare,Medicaid,or other third- party payors that are false or fraudulent;• the federal Health Insurance Portability and Accountability Act of 1996,or HIPAA,which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;• HIPAA,as amended by the Health Information Technology **and** ~~clinical~~ **Clinical** ~~study costs narrowness of the statutory exceptions and safe harbors available,it is possible that some of our business activities could be subject to challenge under one~~ or more of such laws.In addition,recent healthcare reform legislation has strengthened these laws.For example,the Healthcare Reform Law,among other things,amends the intent requirement of the federal anti- kickback and criminal healthcare fraud statutes.A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it.Moreover,the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti- kickback statute constitutes a false or fraudulent claim for purposes of the False Claims **Act.If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to** . If ~~amounts allocated to federal grants were reduced or~~ **our** ~~eliminated~~ **operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us** , we ~~would~~ **may** be ~~required~~ **subject** to ~~fund the shortfall~~ **penalties, including civil and criminal penalties, damages, fines, exclusion from participation** in **government healthcare programs, such as Medicare and Medicaid, imprisonment, and** the ~~ORCA- V1 clinical study costs~~ **curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and its results of operations** . Our employees, independent contractors, consultants, commercial partners, principal investigators, or CROs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have

a material adverse effect on our business. We are exposed to the risk of fraud or misconduct by employees, independent contractors, consultants, commercial partners, principal investigators, or CROs, which could include intentional, reckless, negligent, or unintentional failures to comply with FDA regulations, comply with applicable fraud and abuse laws, provide accurate information to the FDA, report financial information or data accurately, or disclose unauthorized activities to us. This misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter this type of 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, financial condition and results of operations, including the imposition of significant fines or other sanctions. Further, even if we are successful in asserting a defense, we may incur substantial costs in preparing and maintaining our defense and any such action would be time- and resource- intensive and potentially divert management' s attention from the business, which could adversely affect our business and results of operations. **Moreover, our employees are increasingly utilizing social media tools and our website as a means of communication. Despite our efforts to monitor social media communications, there is risk that the unauthorized use of social media by our employees to communicate about our products or business, or any inadvertent disclosure of material, nonpublic information through these means, may result in violations of applicable laws and regulations, which may give rise to liability and result in harm to our business. In addition, there is also risk of inappropriate disclosure of sensitive information, which could result in significant legal and financial exposure and reputational damages that could potentially have a material adverse impact on our business, financial condition, results of operations and prospects. Our employees could also inappropriately utilize artificial intelligence, or AI, in connection with their social media communications, introducing another potential source of reputational damage or other potential legal or financial exposure. A Breakthrough Therapy designation by the FDA may not lead to a faster development or regulatory review or approval process for the vaping / e- cigarette cessation indication and it does not increase the likelihood that our product candidates will receive marketing approval. The FDA has granted Breakthrough Therapy designation for cytisinicline for nicotine e- cigarette, or vaping, cessation. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development but does not guarantee a more efficient path. Our receipt of Breakthrough Therapy designation for cytisinicline may not result in a faster development process, review or approval and does not assure ultimate approval by the FDA. In addition, when a product candidate qualifies as a breakthrough therapy, the FDA may later decide that the product no longer meets the conditions for qualification.** Risks Related to our Business Operations To date our business activities have been focused primarily on the development and regulatory approval of cytisinicline and its various alternative forms. Although we have not generated revenue to date, we expect that, after any regulatory approval, any receipt of revenue will be attributable to sales of cytisinicline, primarily in the United States, the EU (including the U. K.) and Asia. Because we devote substantially all of our resources to the development of cytisinicline and rely on cytisinicline as our sole source of potential revenue for the foreseeable future, any factors that negatively impact this product, or result in decreasing product sales, would materially and adversely affect our business, financial condition and results of operations. Our future success depends in part on our ability to attract, retain, and motivate other qualified personnel. We will need to expand and effectively manage our managerial, operational, financial, development and other resources in order to successfully pursue our development and commercialization efforts for our existing and future product candidates. We expect to need additional scientific, technical, operational, financial and other personnel. Our success depends on our continued ability to attract, retain and motivate highly qualified personnel, such as management, clinical and preclinical personnel, including our executive chairman **Thomas B. King, and our executive officers** Richard Stewart **, Mark Oki** ~~and our executive officers John Bencich~~ , Cindy Jacobs **and** ~~, Anthony Clarke,~~ Jaime Xinos ~~and Craig Donnelly~~ . In addition, although we have entered into employment agreements with each of Mr. **King, Mr.** Stewart, Mr. ~~Bencich~~ **Oki** , Dr. Jacobs **and** ~~, Dr. Clarke,~~ Ms. Xinos ~~and Mr. Donnelly~~ , such agreements permit those executives to terminate their employment with us at any time, subject to providing us with advance written notice. We may not be able to attract and retain personnel on acceptable terms, if at all, given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in development and commercialization of cytisinicline may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of our current personnel may impede the progress of our research, development, and commercialization objectives and would negatively impact our ability to succeed in our product development strategy. We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations. We ~~may~~ **will** need to expand our organization **as we prepare for potential commercialization of cytisinicline** , which may require us to divert a disproportionate amount of our attention away from our day- to- day activities and devote a substantial amount of time to managing these growth activities **. We do not currently have a commercial infrastructure, and we may not be able to successfully develop a commercial infrastructure to support the commercialization of cytisinicline on the timeline needed, or at all. Commercialization requires significantly greater financial and organizational resources, which may not be available to us** . We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in its infrastructure, operational

mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Expanded growth ~~could~~ **and commercialization** ~~require~~ **requires** significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our growth **or commercialize plans** , our expenses may increase more than expected, our ability to generate and / or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth **and commercialization** . In the future, we may invest in the development of additional indications for cytisinicline. If we invest in and are unsuccessful in developing additional indications for cytisinicline, our business, financial condition and results of operations may be adversely affected. In the future, we may invest in the research and development of new indications for cytisinicline to address nicotine ~~addictions~~ **dependence** associated with the use of e- cigarette, or vaping, products. Given their recent introduction, the use of vaping products is not fully understood which may increase the risk of failure in this area ~~. We are pursuing clinical studies in users of e- cigarettes and have been awarded a grant by the NIDA / NIH to evaluate the use of cytisinicline as a treatment for cessation of nicotine e- cigarette use. Continued grant funding under the award will still be subject to availability of funds at the NIDA / NIH, and such funding will not be sufficient to cover the full clinical costs of the Phase 2 ORCA- V1 trial~~ . We expect that we will need to invest significant amounts of capital to pursue development of an e-cigarette cessation indication. If we are unable to provide such additional capital when needed, we may be unable to complete the development, regulatory approval and commercialization of an e- cigarette cessation indication. The development of additional indications for cytisinicline is highly uncertain. During the research and development cycle, we may expend significant time and resources on developing additional indications without any assurance that we will recoup our investments or that our efforts will be commercially successful. A high rate of failure is inherent in the discovery and development of additional indications, and failure can occur at any point in the process, including late in the process after substantial investment. Further, any new indications may not be accepted by physicians and the medical community at large, and competitors may develop and market equivalent or superior products. Failure to launch commercially successful new indications for cytisinicline after significant investment could have a material adverse effect on our business, financial condition and results of operations. Our internal computer systems, or those of our third- party collaborators or other service providers, may fail or suffer security breaches and cyber- attacks, which could result in a material disruption of our development programs. We believe that we take reasonable steps that are designed to protect the security, integrity and confidentiality of the information we collect, use, store, and disclose, but inadvertent or unauthorized data access may occur despite our efforts. Our system protections may be ineffective or inadequate, or we could be impacted by software bugs or other technical malfunctions, as well as employee error or malfeasance. Additionally, privacy and data protection laws are evolving, and it is possible that these laws may be interpreted and applied in a manner that is inconsistent with our data handling safeguards and practices that could result in fines, lawsuits, and other penalties, and significant changes to our or our third- party collaborators or service providers business practices and products and service offerings. To the extent that the measures we or our third- party collaborators or service providers have taken prove to be insufficient or inadequate, we may become subject to litigation, breach notification obligations, or regulatory or administrative sanctions, which could result in significant fines, penalties, damages, harm to our reputation, or loss of customers. While we have not experienced any material losses as a result of any system failure, accident or security breach to date, we have been the subject of certain phishing attempts in the past. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. Additionally, a party who circumvents our security measures could, among other effects, appropriate patient information or other proprietary data, cause interruptions in our operations, or expose our collaborators to hacks, viruses, and other disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, insurance coverage to compensate for any losses associated with such events, if available, may not be adequate to cover all potential losses. The development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. To the extent that any disruption, security breach, or cyber- attack were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidate could be delayed. Depending on the nature of the information compromised, in the event of a data breach or other unauthorized access to our patient data, we may also have obligations to notify patients and regulators about the incident, and we may need to provide some form of remedy, such as a subscription to credit monitoring services, pay significant fines to one or more regulators, or pay compensation in connection with a class- action settlement (including under the new private right of action under the California Consumer Privacy Act of 2018). Such breach notification laws continue to evolve and may be inconsistent from one jurisdiction to another. Complying with these obligations could cause us to incur substantial costs and could increase negative publicity surrounding any incident that compromises customer data. Additionally, the financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we may maintain or obtain in the future, and there can be no assurance that the limitations of liability in any of our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above. Any of the foregoing could have an adverse effect on our business, reputation, financial condition and results of operations. **In efforts to innovate and optimize operational efficiency, certain third parties with whom we work may integrate AI into various aspects of their work with us. While we do not currently utilize AI tools in a significant way, we may in the future integrate AI into various projects. While AI presents opportunities for enhanced productivity and innovation, it also introduces inherent risks, including legal and regulatory, that could adversely impact our business**

and reputation. Proper use of AI can lead to improved decision- making, cost reduction, and competitive advantage. However, improper use, including algorithmic biases, ethical considerations, data privacy issues, unknown or zero- day software vulnerabilities, and potential regulatory non- compliance, by our employees or third parties with whom we work could result in reputational damage, legal liabilities, and financial losses. The rapidly evolving regulatory landscape surrounding AI also poses a risk, as new laws and regulations could impose additional compliance burdens, resulting in increased operational costs. We are committed to implementing robust governance and control mechanisms to mitigate these risks, but there can be no assurance that such measures will adequately prevent or mitigate the adverse effects that the integration and use of AI may have on our business, financial condition, and results of operations. Risks Related to Our Reliance on Third Parties We expect to continue to rely on third parties to manufacture cytisinicline. We currently exclusively rely on Sopharma to manufacture cytisinicline for use in clinical trials and plan to engage other third parties for our manufacturing process, including to manufacture cytisinicline on a commercial scale, if approved. Our commercialization of cytisinicline could be stopped, delayed or made less profitable if Sopharma fails to obtain approval of government regulators, fails to provide us with sufficient quantities of product or fails to do so at acceptable quality levels or prices. We do not currently have, nor do we currently plan to develop, the internal infrastructure or capability to manufacture our clinical supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture cytisinicline on a clinical or commercial scale. We currently exclusively rely on Sopharma to manufacture cytisinicline for use in clinical trials and plan to engage other third parties for our manufacturing process, including, if cytisinicline is approved, to manufacture cytisinicline on a commercial scale, with tableting, blistering and packaging. We may encounter technical difficulties or delays in the transfer of cytisinicline manufacturing on a commercial scale to other third- party manufacturers, encounter difficulties and delays in identifying third- party manufacturers other than Sopharma. We may be unable to enter into agreements for commercial supply with third- party manufacturers on acceptable terms, or at all **. If and when product sales for cytisinicline commence and grow, cytisinicline 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, or we otherwise experience a product shortfall, any such product shortfall could delay commercialization of cytisinicline and impair sales, and our business, financial condition and results of operations could be materially adversely affected** . Sopharma and potential other third- party manufacturers are subject to regulatory requirements covering manufacturing, testing, quality control and record keeping relating to product candidates and are also subject to ongoing inspections by regulatory agencies. While Sopharma has been subject to oversight by regulators in Europe and Bulgaria, they have never been inspected by the FDA and there is no assurance that their quality systems will be satisfactory to pass a pre-approval inspection by the FDA. Failure by Sopharma or any of our potential third- party manufacturers to comply with applicable regulations may result in long delays and interruptions to our product candidate supply while we seek to secure another supplier that meets all regulatory requirements. Our reliance on Sopharma and potential other third- party manufacturers exposes us to the following additional risks: • Sopharma and potential other third- party manufacturers might be unable to timely manufacture cytisinicline or produce the quantity and quality required to meet our clinical and commercial needs, if any; • Sopharma and potential other third- party manufacturers may not be able to execute our manufacturing procedures appropriately; • Sopharma and potential other third- party manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products; • Sopharma and potential other third- party manufacturers are or will be subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMPs and other government regulations and corresponding foreign standards. We do not have control over Sopharma' s, or other third parties', compliance with these regulations and standards; • we may not own, or may have to share, the intellectual property rights to any improvements made by Sopharma and potential other third- party manufacturers in the manufacturing process for cytisinicline; • we do not own all the intellectual property rights to cytisinicline, and Sopharma and potential other third- party manufacturers could license such rights to third parties or begin supplying other third parties with cytisinicline; and • Sopharma and potential other third- party manufacturers could breach or terminate their agreement with us. Each of these risks could delay our clinical trials, the approval, if any, of cytisinicline by the FDA or the commercialization of cytisinicline or result in higher costs or deprive us of potential product revenue. We **currently** rely on **Sopharma** ~~third party contract manufacturing organizations, or CMOs,~~ to package the cytisinicline used in our clinical trials. If **Sopharma** ~~any of these CMO' s fail~~ **fails** to timely deliver the supplies needed, then our clinical studies could be delayed materially. **Sopharma** ~~Third- party manufacturers~~ may fail to perform under their contractual obligations or may fail to deliver the required commercial product on a timely basis and at commercially reasonable prices. If we are required to identify and qualify an alternate manufacturer, we may be forced to delay or suspend our clinical trials ~~. We expect to continue to depend on third- party contract manufacturers for the foreseeable future~~ . The manufacture of medical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of medical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in the supply of cytisinicline or in the Sopharma manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot be assured that any stability or other issues relating to the manufacture of cytisinicline will not occur in the future. Additionally, Sopharma may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or political instability in the countries in which Sopharma conducts its operations. For example, the military

conflict between Russia and Ukraine may increase the likelihood of supply interruptions and hinder our ability to find the materials we need to make our product candidate. If Sopharma were to encounter any of these difficulties, or otherwise fail to comply with its contractual obligations, our ability to provide our product candidate to patients in clinical trials could be delayed or suspended. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Similar political instability could also harm the commercial production and supply of cytisinicline in the event that cytisinicline is ultimately approved for commercial sale. In June 2021, Pfizer Inc. halted the distribution of its smoking cessation drug, Chantix (varenicline) ~~,~~ after heightened levels **of a nitrosamine impurity** , **called N- nitroso- varenicline, which were** above the FDA' s acceptable daily intake limit, ~~of nitrosamines~~ were found in some lots of Chantix pills **. Long- term use of products containing N- nitroso- varenicline may be associated with a potential increased cancer risk in humans** . In September 2021, Pfizer announced a nationwide recall in the United States of all lots of Chantix and have also withdrawn the product in other countries around the globe. We have undertaken a review of cytisinicline in accordance with regulatory guidance to assess the risk of the presence of ~~nitrosamine~~ **nitrosamines** and other potential impurities. If contaminants, or impurities **We and our third- party manufacturers may also be impacted by new legislation and regulations relating to the manufacture of medical products. For example, legislation has been introduced and passed in Congress to limit certain U. S. biotechnology companies from using equipment or services produced or provided by select Chinese biotechnology companies, including those affiliated with the manufacture of our API, Wuxi STA, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U. S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to** such **actions** ~~as nitrosamines, are discovered in quantities above regulators' thresholds within our~~ - **or what actions** ~~supply of cytisinicline, we~~ may **be taken by the other countries in retaliation** ~~potentially delay product development and approval or have a material adverse impact on our business~~ . We rely on third parties to conduct our clinical trials and perform other services. If these third parties do not successfully perform and comply with regulatory requirements, we may not be able to successfully complete clinical development, obtain regulatory approval or commercialize cytisinicline and our business could be substantially harmed. We plan to rely upon third- party CROs to conduct, monitor and manage our ongoing clinical programs. We rely on these parties for execution of clinical trials and manage and control only some aspects of their activities. We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable laws, regulations and guidelines, including those required by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. If we or any of our CROs or vendors fail to comply with applicable laws, regulations and guidelines, the results generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be assured that our CROs and other vendors will meet these requirements, or that upon inspection by any regulatory authority, such regulatory authority will determine that efforts, including any of our clinical trials, comply with applicable requirements. Our failure to comply with these laws, regulations and guidelines may require us to repeat clinical trials, which would be costly and delay the regulatory approval process. If any of our relationships with these third- party CROs terminate, we may not be able to enter into arrangements with alternative CROs in a timely manner or do so on commercially reasonable terms. In addition, our CROs may not prioritize our clinical trials relative to those of other customers and any turnover in personnel or delays in the allocation of CRO employees by the CRO may negatively affect our clinical trials. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, continued development of cytisinicline may be delayed or terminated and we may not be able to meet our current plans with respect to cytisinicline. CROs may also involve higher costs than anticipated, which could negatively affect our financial condition and operations. We may not be able to establish or maintain the third- party relationships that are necessary to develop or potentially commercialize cytisinicline. Our business plan relies heavily on third - party collaborators, partners, licensees, clinical research organizations, clinical investigators, vendors or other third parties to support our research and development efforts and to conduct clinical trials for cytisinicline. We cannot guarantee that we will be able to successfully negotiate agreements for, or maintain relationships with, these third parties on a commercially reasonable basis, if at all. If we fail to establish or maintain such third- party relationships as anticipated, our business could be adversely affected. We may be unable to realize the potential benefits of any collaborations which we may enter into with other companies for the development and commercialization of cytisinicline. We may enter into a collaboration with third parties concerning the development and / or commercialization of cytisinicline; however, there is no guarantee that any such collaboration will be successful. Collaborations may pose a number of risks, including: • collaborators often have significant discretion in determining the efforts and resources that they will apply to the collaboration, and may not commit sufficient resources to the development, marketing or commercialization of cytisinicline; • collaborators may not perform their obligations as expected; • any such collaboration may significantly limit our share of potential future profits from the associated program, and may require us to relinquish potentially valuable rights to cytisinicline, or other potential products or proprietary technologies or grant licenses on terms that are not favorable to us; • collaborators may cease to devote resources to the development or commercialization of cytisinicline if the collaborators view cytisinicline as competitive with their own products or product candidates; • disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of cytisinicline, and might result in legal proceedings, which would be time consuming, distracting and expensive; • collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could

cause them to divert resources away from the collaboration; • collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; • the collaborations may not result in us achieving revenues to justify such transactions; and • collaborations may be terminated and, if terminated, may result in a need for us to raise additional capital to pursue further development or commercialization of cytisinicline. As a result, a collaboration may not result in the successful development or commercialization of cytisinicline. We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations. In the normal course of business, we enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreement. With respect to our collaboration agreements, we indemnify our collaborators from any third- party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consultants, we indemnify them from claims arising from the good faith performance of their services. Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected. We may rely on third parties to perform many essential services for any of our current or future product candidates that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize any of our current or future product candidates will be significantly impacted and we may be subject to regulatory sanctions. We may retain third - party service providers to perform a variety of functions related to the sale and distribution of any of our current or future product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, and cash collection, and, as a result, most of our inventory may be stored at a single warehouse maintained by one such service provider. If we retain a service provider, we would substantially rely on it as well as other third - party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third - party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action. In addition, we may engage third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements related to adverse event reporting, we could be subject to regulatory sanctions. Additionally, if a third- party errs in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability and potentially cause government programs to overpay providers for our products, which could expose us to significant False Claims Act liability and other civil monetary penalties. Risks Related to Commercialization of Cytisinicline We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us. The development and commercialization of new products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to products for smoking cessation and other product candidates that we may seek to develop or commercialize in the future. We are aware that many companies have therapeutics marketed or in development for smoking cessation. We expect that our competitors and potential competitors have historically dedicated, and will continue to dedicate, significant resources to aggressively develop and commercialize their products in order to take advantage of the significant market opportunity. We have and will continue to pursue new cytisinicline products and alternative sources of cytisinicline used for our products, including additional natural and synthetic sources and routes. The pursuit and development of alternative cytisinicline products and sources is expensive, time consuming, involves significant risk and may not be commercially feasible. There is no guarantee that we will be successful, or that we will be able to develop new products or alternative cytisinicline sources first before our competitors do. Many of our competitors have substantially greater financial, name recognition, manufacturing, marketing, research, technical and other resources than us. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Further, our competitors may develop new products that are safer, more effective or more cost- efficient than cytisinicline. Large pharmaceutical companies in particular have extensive expertise in non- clinical and clinical testing and in obtaining regulatory approvals for products. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Failure of cytisinicline to effectively compete against established treatment options or in the future with new products currently in development would harm our business, financial condition, results of operations and prospects. The commercial success of cytisinicline will depend upon the degree of market acceptance by physicians, patients, third- party payors, and others in the medical community. Failure to obtain or maintain adequate reimbursement or insurance coverage for

products, if any, could limit our ability to market cytisinicline and decrease our ability to generate revenue. Even with the approvals from the FDA and comparable foreign regulatory authorities, the commercial success of cytisinicline will depend in part on the healthcare providers, patients, and third- party payors accepting cytisinicline as medically useful, cost- effective, and safe. Cytisinicline may not gain market acceptance by physicians, patients and third- party payors. The degree of market acceptance of cytisinicline will depend on a number of factors, including but not limited to: • the safety and efficacy of cytisinicline as demonstrated in clinical trials and potential advantages over competing treatments, if any; • the clinical indications for which approval is granted, if any, including any limitations or warnings contained in cytisinicline' s approved labeling; • the cost of treatment; • the perceived ratio of risk and benefit of these therapies by physicians and the willingness of physicians to recommend the product to patients based on such risks and benefits; • the marketing, sales and distribution support for cytisinicline; • the publicity concerning cytisinicline or competing products and treatments; • the pricing and availability of third- party insurance coverage and reimbursement; • negative perceptions or experiences with our competitor' s products may be ascribed to cytisinicline; and • availability of cytisinicline from other suppliers and / or distributors. Even if cytisinicline displays a favorable efficacy and safety profile upon approval, market acceptance of cytisinicline remains uncertain. Efforts to educate the medical community and third- party payors on the benefits of cytisinicline, if any, may require significant investment and resources and may never be successful. ~~Additionally~~ **Sales of cytisinicline** , **if any, will depend substantially, both domestically and abroad, on the extent to which the costs of cytisinicline will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. Significant uncertainty exists as to the reimbursement status for newly approved prescription products, including coding, coverage and payment. There is no uniform policy requirement for coverage and reimbursement for prescription products among** third- party payors **in** ~~, including governmental and private insurers, may also encourage~~ the ~~use of generic~~ **United States; therefore, coverage and reimbursement for our** products **could differ significantly from payor** ~~instead of cytisinicline, or a generic version of cytisinicline, which require a prescription or may be available OTC. If our products fail~~ to **payor. In the United States** ~~achieve an adequate level of acceptance by physicians, patients~~ , third- party payors **often rely upon Medicare** ~~, and other healthcare providers, we will not be able to generate sufficient revenue to become or remain profitable. The pricing,~~ coverage **policy** ~~, and reimbursement of cytisinicline, if any, must be sufficient to support our commercial efforts and other development programs and the availability and adequacy of coverage and reimbursement by third- party payors, including governmental and private insurers, are essential for most patients to be able to afford treatments. Sales of cytisinicline, if any, will depend substantially, both domestically and abroad, on the extent to which the costs of cytisinicline will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide cytisinicline for free or we may not be able to successfully commercialize cytisinicline. In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new products are typically made by the Centers for Medicare and Medicaid Services, or CMS, an~~ **and** ~~agency within~~ **payment limitations in setting** ~~the~~ **their own** ~~U. S. Department of Health and Human Services, as CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow the coverage~~ reimbursement policies ~~established by CMS to a substantial degree~~ **, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations** . It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates such as cytisinicline and what reimbursement codes cytisinicline may receive if approved. **If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide cytisinicline for free or we may not be able to successfully commercialize cytisinicline Additionally, third- party payors, including governmental and private insurers, may also encourage the use of generic products instead of cytisinicline, or a generic version of cytisinicline, which require a prescription or may be available OTC. If our products fail to achieve an adequate level of acceptance by physicians, patients, third- party payors, and other healthcare providers, we will not be able to generate sufficient revenue to become or remain profitable.** Outside the United States, selling operations are generally subject to extensive governmental price controls and other price- restrictive regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of products. In many countries, the prices of products are subject to varying price control mechanisms as part of national health systems. Price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products, if any. Accordingly, in markets outside the United States, the potential revenue may be insufficient to generate commercially reasonable revenue and profits. **To secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost- effectiveness of the product to third- party payors, which costs would be in addition to those required to obtain FDA or other comparable regulatory approvals. A payor' s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved.** Moreover, ~~,~~ eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs.Interim payments for new products,if applicable,may also not be sufficient to cover our costs and may not be made permanent.Payment rates may vary according to the use of the product and the clinical setting in which it is used,may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services.Net prices for products may be reduced by mandatory discounts or rebates required by third- party payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States.Accordingly,the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each

payor separately,with no assurance that coverage and adequate payment will be applied consistently or obtained.The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product.Even if reimbursement is provided,market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for health care providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use **.** ~~increasing~~ **Increasing efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products. Increasing** efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with products due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription products, has and is expected to continue to increase in the future. As a result, profitability of cytisinicline, if any, may be more difficult to achieve even if regulatory approval is received **.The** containment of health care costs has become a priority of federal and state governments and the prices of drug products have been a focus in this effort.For example,there have been several recent U.S.Congressional inquiries and proposed bills designed to,among other things,bring more transparency to drug pricing,review the relationship between pricing and manufacturer patient programs,and reform government program reimbursement methodologies for drugs.We expect that federal,state and local governments in the United States will continue to consider legislation directed at lowering the total cost of health care.Individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing,including price or patient reimbursement constraints,discounts,restrictions on certain product access and marketing cost disclosure and transparency measures,and,in some cases,designed to encourage importation from other countries and bulk purchasing.In December 2020,the U.S.Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers and other members of the health care and pharmaceutical supply chain,an important decision that may lead to further and more aggressive efforts by states in this area. ~~The Biden Administration has indicated that lowering prescription drug prices is a priority,but we do not yet know what steps the administration will take or whether such steps will be successful.~~ It is uncertain whether and how future legislation or regulatory changes,to the ACA and otherwise,could affect prospects for our product candidates or what actions third- party payors may take in response to any such health care reform proposals or legislation.Adoption of price controls and cost containment measures,and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue,attain profitability or commercialize our product candidates.Currently,the ACA and other federal laws and rules require most health insurance plans in the United States to cover some level of tobacco cessation treatments,including smoking cessation counseling and medications.If these provisions are repealed,in whole or in part,our business,financial condition,or results of operations could be negatively affected.Failure by us or a commercial partner to obtain timely or adequate coverage and pricing **for our products,if approved,or obtaining such coverage and pricing at unfavorable levels,could materially adversely affect our business,financial conditions,results of operations and prospects** . Sopharma may breach its supply agreement with us and sell cytisinicline into our territories or permit third parties to export cytisinicline into our territories and negatively affect our commercialization efforts of our products in our territories. We are currently dependent on the exclusivity provisions of our supply agreement with Sopharma to conduct our business and to prevent Sopharma from competing, directly and indirectly, with us in the United States and Western Europe. If Sopharma were to breach the exclusivity provisions of the supply agreement with us and sell or distribute cytisinicline directly into our territories or permit third parties to export cytisinicline into our territories, among other things, the increase in competition within our anticipated markets could have a material adverse effect on our business, results of operations and financial condition. The illegal distribution and sale by third parties of counterfeit versions of cytisinicline, stolen products, or alternative third- party distribution and sale of cytisinicline could have a negative impact on our financial performance or reputation. Cytisinicline is not eligible for composition of matter patents in the United States as it is a naturally occurring substance. As such, third parties are able to manufacture, sell or distribute cytisinicline without royalties or other payments to us and compete with our products in the United States and potentially worldwide and negatively impact our commercialization efforts of our products. We are aware of additional cytisinicline products approved in several European countries and we may not be able to block other third parties from launching generic versions of cytisinicline. Third parties may also sell or distribute cytisinicline as an herbal or homeopathic product. Other than regulatory exclusivity or other limitations, there may be little to nothing to stop these third parties from manufacturing, selling or distributing cytisinicline. Because we have no ability to set rigorous safety standards or control processes over third **-** party manufacturers, sellers or distributors of cytisinicline, excluding Sopharma, these formulations of cytisinicline may be unsafe or cause adverse effects to patients and negatively impact the reputation of cytisinicline as a safe and effective smoking cessation aid. Third parties could illegally distribute and sell counterfeit versions of cytisinicline, especially on online marketplaces, which do not meet the rigorous manufacturing and testing standards under cGMP. Counterfeit products are frequently unsafe or ineffective, and may even be life- threatening. Counterfeit medicines may contain harmful substances, the wrong dose of the active pharmaceutical ingredient or no active pharmaceutical ingredients at all. However, to distributors and users, counterfeit products may be visually indistinguishable from the authentic version. Reports of adverse reactions to counterfeit products, increased levels of counterfeiting, or unsafe cytisinicline products could materially affect patient confidence in our cytisinicline product. It is possible that adverse events caused by unsafe counterfeit or other cytisinicline products that we do not produce will mistakenly be attributed to our cytisinicline product. In addition, thefts of inventory that are not properly stored at warehouses, plants or while in- transit, and which are sold through unauthorized channels could adversely impact patient safety, our reputation, and our business. Public loss of confidence in the integrity in

cytisinicline as a result of counterfeiting, theft, or improper manufacturing processes could have a material adverse effect on our business, results of operations, and financial condition. It is illegal to sell unapproved prescription medicines in the United States. Sopharma' s cytisinicline brand is currently approved for sale in certain Central and Eastern European countries. Cytisinicline has not yet received a marketing approval from the FDA, and we intend to conduct the requisite clinical trials to obtain approval for the marketing of cytisinicline in the United States and in major global markets. We are aware that products purporting to be Sopharma' s cytisinicline brand are available, via third - party internet sites, for importation in the United States and other global markets. We have no control over the authenticity of products purchased through these sites, which may be counterfeit or sourced from distributors in Central and Eastern Europe without authorization to sell into the United States or EU. We may attempt to form collaborations in the future with respect to cytisinicline, but we may not be able to do so, which may cause us to alter our development and commercialization plans. We may attempt to form strategic collaborations, create joint ventures or enter into licensing arrangements with third parties with respect to our programs that we believe will complement or augment our existing business. We may face significant competition in seeking appropriate strategic collaborators, and the negotiation process to secure appropriate terms is time consuming and complex. We may not be successful in our efforts to establish such a strategic collaboration for cytisinicline on terms that are acceptable to us, or at all. This may be because cytisinicline may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, the competitive or intellectual property landscape may be viewed as too intense or risky, or cytisinicline' s patent protection insufficient, and / or third parties may not view cytisinicline as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile. Any delays in identifying suitable collaborators and entering into agreements to develop and / or commercialize cytisinicline could delay the development or commercialization of cytisinicline, which may reduce our competitiveness even if we reach the market. Absent a strategic collaborator, we would need to undertake development and / or commercialization activities at our own expense. If we elect to fund and undertake development and / or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our product candidate cytisinicline or bring it to market and our business may be materially and adversely affected. Even if we obtain regulatory approval in....., results of operations and prospects. We may not be successful in any efforts to identify, license, discover, develop, or commercialize additional product candidates. Although a substantial amount of our effort will focus on clinical testing, approval, and potential commercialization of cytisinicline, our sole product candidate, the success of our business is also expected to depend in part upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following: • our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates; • we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates; • our potential product candidates may not succeed in non- clinical or clinical testing; • our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; • competitors may develop alternatives that render our potential product candidates obsolete or less attractive; • potential product candidates we develop may be covered by third parties' patents or other exclusive rights; • the market for a potential product candidate may change during our program so that such a product may become unreasonable to continue to develop; • a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a potential product candidate may not be accepted as safe and effective by patients, the medical community, or third- party payors. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business, financial condition or results of operations and could potentially cause us to cease operations. **We are subject to U. S. and certain foreign export and import controls, sanctions, embargoes, anti- corruption laws, and anti- money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations that can harm our business. We are subject to export control and import laws and regulations, including the U. S. Export Administration Regulations, U. S. Customs regulations, various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls, the U. S. Foreign Corrupt Practices Act of 1977, as amended, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, the USA PATRIOT Act, and other state and national anti- bribery and anti- money laundering laws in the countries in which we conduct activities. Anti- corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We currently have an agreement with Sopharma to supply cytisinicline, and we may engage third parties for clinical trials outside of the United States, to sell our products abroad or provide other services in connection with commercialization, and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud**

litigation, reputational harm, and other consequences. Risks Related to our Intellectual Property ~~Presently, we have rights to intellectual property through trade secrets, licenses, patents from third parties, and patents and applications that we own. Our product candidate may require specific formulations to work effectively and efficiently, and these rights may be held by others. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third- party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to third- party intellectual property rights, our business, financial condition and prospects for growth could suffer.~~ If we are unable to maintain effective proprietary rights for our product candidate or any future product candidates, we may not be able to compete effectively in our proposed markets. We currently rely primarily on trade secret protection and on confidentiality agreements to protect proprietary know- how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know- how, information or technology that is not covered by patents. Trade secrets can be difficult to protect, however, and even where they are protected, they generally provide less intellectual property protection to the holder of the trade secret than to a holder of a patent. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While 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. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know- how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business, financial condition or results of operations. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Third- party claims of intellectual property infringement may prevent or delay our development and commercialization efforts. We are currently developing cytisinicline in treating nicotine dependence for smoking cessation in adults. Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technology without infringing the patent rights of third parties. We are not aware of any patents or patent applications that would prevent the development, manufacture or marketing of cytisinicline for smoking cessation. We are aware of U. S. and foreign patents and pending patent applications owned by third parties that cover certain other therapeutic uses of cytisinicline. We are currently monitoring these patents and patent applications. We may in the future pursue available proceedings in the United States and foreign patent offices to challenge the validity of these patents and patent applications. In addition, or alternatively, we may consider whether to seek to negotiate a license of rights to technology covered by one or more of such patents and patent applications for these certain additional therapeutic uses. If any third- party patents or patent applications cover our product candidates or technologies in other therapeutic uses, we may not be free to manufacture or market our product candidates for additional therapeutic uses, absent such a license, which may not be available to us on commercially reasonable terms, or at all. It is also possible that we have failed to identify relevant third- party patents or applications. For example, applications filed before November 29, 2000 and applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third- party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third- party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to specified limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the U. S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidate. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidate may be subject to claims of infringement of the patent rights of third parties. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we

may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. We intend to rely on patent rights for certain aspects of our product candidates and certain future product candidates. If we are unable to obtain or maintain an adequate proprietary position from this approach, we may not be able to compete effectively in our markets. Although we rely or will rely in part on trade secret protection as part of our intellectual property rights strategies, we also intend to rely on patent rights to protect certain aspects of our technologies and upon the patent rights of third parties from which we license certain of our technologies. We have sought to protect our proprietary position by filing patent applications in the United States and certain other countries around the world related to future product candidates. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or at all. 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. The patent position of pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patent applications or our patents (once issued) have been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our future product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our future product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any future product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a future product candidate under patent protection could be reduced. If we cannot obtain and maintain effective protection of exclusivity from our regulatory efforts and intellectual property rights, including patent protection or data exclusivity, for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed. Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and is therefore costly, time- consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide- ranging patent reform legislation. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained, if any. Depending on decisions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U. S. Supreme Court held that certain claims to naturally occurring substances are not patentable. Cytisinicline is a naturally occurring product and is not patentable. Our intellectual property strategy involves novel formulations of cytisinicline and there is no guarantee that such patents will be issued or if issued, will be broad enough to prevent competitors from developing competing cytisinicline products. Although we do not believe that any patents that may issue from our pending patent applications directed at our product candidate, if issued in their currently pending forms, as well as patent rights licensed by us, will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U. S. Congress or the USPTO may impact the value of our patent rights. There could be similar changes in the laws of foreign jurisdictions that may impact the value of our patent rights or our other intellectual property rights. We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we have written agreements and make every effort to ensure that our employees, consultants, and independent contractors do not use the proprietary information or intellectual property rights of others in their work for us, we may in the future be subject to any claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. 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. It is difficult and costly to protect our proprietary rights and as a result we may not be able to ensure their protection. In addition, patents have a limited lifespan and will eventually expire. Market exclusivity awarded by the FDA upon the approval of an NDA is limited in scope and duration. Our commercial success will depend in part on obtaining, maintaining, enforcing, and defending against third - party challenges, patent and trade secret protection for our current and future product candidates that we may develop, license or acquire, as well as the related manufacturing methods. We will be able to protect our technologies from unauthorized use by third parties to the extent that the technologies are covered by valid and enforceable patents or trade secrets. The patent prosecution process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable 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. Moreover, should we enter into additional collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance, and enforcement of our patent applications and patents. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents and patent applications or in third - party patents and patent applications. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the patent application process is also subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting any of our current or future product candidates that we may develop, license, or acquire by obtaining and defending patents. For example: • we may not have been the first to conceive of and reduce to practice the inventions covered by each of our pending patent applications and issued patents; • we may not have been the first to file patent applications for these inventions; • others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies; • it is possible that none of the pending patent applications will result in issued patents; • the issued patents may not cover commercially viable active products, may not provide us with any competitive advantages, or may be successfully challenged by third parties; • we may not develop additional proprietary technologies that are patentable; • patents of others may have an adverse effect on our business; • noncompliance with requirements of governmental patent agencies 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, potentially allowing competitors to enter the market earlier than would otherwise have been the case; • our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential product candidates; or • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of available patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns. Patents have a limited lifespan. In most countries, including the United States, the expiration of a patent is typically 20 years from the date that the application for the patent is filed. Various extensions of patent term may be available in particular countries; however, in all circumstances the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits a patent term extension of up to five years to cover an FDA - approved product. The actual length of the extension will depend on the amount of patent term lost while the product was in clinical trials. However, the applicable authorities, including the USPTO and the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data, and then may be able to launch their product earlier than might otherwise be the case. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent prosecution process. Periodic maintenance fees, renewal fees, annuity fees, and various other governmental fees on patents or patent applications will be due to be paid to the USPTO and various patent agencies outside of the United States in several stages over the lifetime of the patents and applications. We have systems in place to remind us to pay these fees, and we employ and rely on reputable law firms and other professionals to effect payment of these fees to the USPTO and non - U. S. patent agencies for the patents and patent applications we own and those that we in - license. We also employ reputable law firms and other professionals to help us comply with the various documentary and other procedural requirements with respect to the patents and patent applications that we own and those that we in - license. In some 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 noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. 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. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Competitors may infringe our issued patents, our in- licensed patents, or other intellectual property that we own or in- license. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part; construe the patent' s claims narrowly; or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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. Most of our competitors are larger than we are and have substantially greater resources than we do. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in- license needed technology, or enter into development partnerships that would help us bring our product candidates to market. We or our licensors may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting, and defending patent applications and patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement rights are not as strong as those in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our or our licensors' intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Risks Related to Our Common Stock The price for our common stock is volatile. The market prices for our common stock and that of pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include: • our ability to raise additional capital, the terms of such capital, and our ability to continue as a going concern; • the ability of us or our partners to develop cytisinicline and other product candidates and conduct clinical trials that demonstrate such product candidates are safe and effective; • the ability of us or our partners to obtain regulatory approvals for cytisinicline or other product candidates, and delays or failures to obtain such approvals; • failure of any of our product candidates to demonstrate safety and efficacy, receive regulatory approval and achieve commercial success **; • the ability of us to establish a commercial infrastructure and complete other pre- commercialization and commercialization tasks to necessary to successfully commercialize cytisinicline should it be approved by the FDA** ; • failure to maintain our existing third- party license, manufacturing and supply agreements; • failure by us or our licensors to prosecute, maintain, or enforce our intellectual property rights; • changes in laws or regulations applicable to our candidates; • any inability to obtain adequate supply of product candidates or the inability to do so at acceptable prices; • adverse regulatory authority decisions; • introduction of new or competing products by our competitors; • failure to meet or exceed financial and development projections we may provide to the public; • the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community; • announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors; • disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain intellectual property protection for our technologies; • additions or departures of key personnel; • significant lawsuits, including intellectual property or stockholder litigation; • if securities or industry analysts do not publish research or reports about us, or if they issue an adverse or misleading opinion regarding our business and stock; • changes in **federal or global health policies, legislation or the review and oversight functions of federal health regulatory bodies; • changes in** the market valuations of similar companies; • general market or macroeconomic conditions and geopolitical conditions, including **fluctuating inflation, interest and tariff rates, increased volatility in** the ~~current~~ **debt and equity markets, instability in the** global ~~economic recession~~ **banking system** , ~~increasing inflation and interest rates, and the increasingly volatile~~ global ~~economic conditions resulting from global~~ **health crises and pandemics and geopolitical** ~~conflicts~~ - **conflict, and their potentially material adverse impact on our business and the execution of our preclinical studies and clinical trials** ; • sales of our common stock us or our stockholders in the future; • trading volume of our common stock; • adverse publicity relating to our markets generally, including with respect to other products and potential products in such markets; • changes in the structure of healthcare payment systems; • period- to- period fluctuations in our financial results; and • tweets or other social media posts related to our market and industry. Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. An increase in the market price of our common stock, which is uncertain and unpredictable, may be the sole source of gain from an investment in our common stock. An investment in our common stock may not be appropriate for investors who require dividend income. We have never declared or paid cash dividends on our capital stock and do not anticipate paying any cash dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for stockholders for the foreseeable future. Accordingly, an investment in our common stock may not be appropriate for investors who require dividend income or investors who are not prepared to bear a significant risk of losses from such an investment. A significant portion of

our total outstanding shares of common stock may be sold into the public market at any point, which could cause the market price of our common stock to drop significantly, even if our business is doing well, and result in significant dilution to our stockholders. Sales of a substantial number of shares of our common stock in the public market could occur at any time, either by us or our stockholders. These sales, or the perception in the market that we or holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent such shares have already been registered under the Securities Act and are held by non- affiliates. In ~~May~~ **July** ~~2023~~ **2024**, we entered into the **New** ~~$ 16. 6 million~~ Debt Agreement with the Lenders **for term loans of up to $ 20. 0 million**. Subject to certain terms and conditions, the Lenders may convert all or any part of the outstanding **New** Convertible Term Loan and accrued and unpaid interest at any time prior to maturity into shares of our common stock at a conversion price equal to **(i) for the first tranche of** $ ~~9~~ **10**. ~~34~~ **0 million, $ 7. 00** per share, subject to customary anti- dilution adjustments **and (ii) for the second and third tranches of $ 5. 0 million each, the greater of (x) $ 4. 854 per share, subject to customary anti- dilution adjustments, and (y) the lower of (a) 150 % of the average of the closing sale price of our common stock during the 10 trading days preceding the effective date of such tranche and (b) 150 % of the closing sale price of our common stock on the trading day immediately preceding the effective date of such tranche**. Additionally, all outstanding amounts under the **New** Convertible Term Loan, including accrued and unpaid interest, will mandatorily convert into shares of our common stock, at the conversion price, on such date, if any, when the closing price per share of our common stock has been **(i) for the first tranche,** equal to or greater than $ 24. 00 for **30 consecutive trading days prior to such date and (ii) for the second and third tranches, three times the applicable conversion price for such tranche, in each case, for the** 30 consecutive trading days prior to such date. We are aware that there can be no assurance that the **New Convertible** Term ~~Loans~~ **Loan** will be available to us for borrowing nor whether the ~~Lenders~~ **Lender** will be willing to work with us on any modifications to the current **New** Convertible Term Loan or **the New** Debt Agreement. As of December 31, ~~2023~~ **2024**, there were ~~1~~ **2**, ~~461~~ **139**, ~~980~~ **414** shares of our common stock subject to outstanding options and ~~507~~ **1**, ~~875~~ **283, 750** subject to outstanding restricted stock units, almost all of which have been registered under the Securities Act on Form S- 8. The shares so registered can be freely sold in the public market after being issued to the option holder upon exercise, except to the extent they are held by an affiliate of ours, in which case such shares will become eligible for sale in the public market as permitted by Rule 144 under the Securities Act. Furthermore, as of December 31, ~~2023~~ **2024**, there were approximately ~~4, 946, 171~~ **17, 521, 398** shares of our common stock subject to outstanding warrants to purchase common stock, with a weighted average exercise price of $ 5. ~~48~~ **15** per share, and 142, 857 shares of our common stock subject to outstanding pre- funded warrants, with an exercise price of $ 0. 001 per share. To the extent any of these warrants are exercised, the shares underlying these warrants may be immediately sold in the public market. In February 2024, we announced the sale and issuance of warrants to purchase up to 13, 086, 151 shares of common stock (or pre- funded warrants), with an exercise price of $ 4. 906 per share (or $ 4. 905 per pre-funded warrant), in a concurrent private placement with the sale of 13, 086, 151 shares of common stock sold in a registered direct offering. We ~~expect to register~~ **registered** the shares underlying these warrants (or pre- funded warrants) for resale **on Form S- 3, which was declared effective on May 6, 2024**. If ~~, following such registration,~~ these shares are issued upon exercise of the warrants (or pre- funded warrants), they may be immediately sold in the public market. The sale of additional shares of our common stock, the conversion of the **New** Convertible Term Loan into shares of our common stock, the exercise of any of our outstanding warrants, the exercise of any of our outstanding options, or the settlement of our restricted stock units would have a dilutive impact on our existing stockholders and could cause the market price of our common stock to decline significantly. Sales of our common stock, the conversion of the **New** Convertible Term Loan, the exercise of any of our outstanding warrants, the exercise of any of our outstanding options, the settlement of our restricted stock units or the perception that such events will occur, could also encourage short sales by third parties, which could contribute to the further decline of the price of our common stock. Additionally, the sale of a substantial number of shares of our common stock, the conversion of the **New** Convertible Term Loan, the exercise of any of our outstanding warrants, the exercise of any of our outstanding options, the settlement of our restricted stock units or the perception that such events will occur, could make it more difficult for us to sell equity or equity- related securities in the future at a time and at a price that we might otherwise wish. In addition, in the future, we plan to raise additional capital through private placements or public offerings of our equity or debt securities. We cannot be certain that additional funding will be available on acceptable terms, if at all. To the extent that we raise additional financing by issuing equity securities, we may do so at a price per share that represents a discount to the then- current per share trading price of our common stock and our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants, such as limitations on our ability to incur additional indebtedness, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely affect our ability to conduct our business. Because our merger resulted in an ownership..... business or stock price to suffer. If we raise additional capital, the terms of the financing transactions may cause dilution to existing stockholders or contain terms that are not favorable to us. In the future, we plan to raise additional capital through private placements or public offerings of our equity or debt securities. We cannot be certain that additional funding will be available on acceptable terms, if at all. To the extent that we raise additional financing by issuing equity securities, we may do so at a price per share that represents a discount to the then- current per share trading price of our common stock and our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants, such as limitations on our ability to incur additional indebtedness, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely affect our ability to conduct our business . Shareholder activists could cause a disruption..... with resolving such action in other jurisdictions. We are a smaller reporting company and we cannot be certain if the reduced disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors. We are currently a " smaller reporting company " as defined in the Exchange Act,

and are thus allowed to provide simplified executive compensation disclosures in our filings, are exempt from the provisions of Section 404 (b) of the Sarbanes- Oxley Act requiring that an independent registered public accounting firm provide an attestation report on the effectiveness of internal control over financial reporting and have certain other decreased disclosure obligations in our SEC filings. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. ~~well as rules implemented by the SEC and The Nasdaq Capital Market.These rules and regulations impose significant legal and financial compliance costs and make some activities more time- consuming and costly.In addition,it may be difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers,which may adversely affect investor confidence and could cause our business or stock price to suffer~~ .Shareholder activists could cause a disruption to our business.An activist investor may indicate disagreement with our strategic direction or capital allocation policies and may seek representation on our board of directors.Our business,operating results or financial condition could be adversely affected and may result in,among other things:• increased operating costs,including increased legal expenses,insurance,administrative expenses and associated costs incurred in connection with director election contests;• uncertainties as to our future direction,which could result in the loss of potential business opportunities and could make it more difficult to attract,retain,or motivate qualified personnel,and strain relationships with investors and customers;and • reduction or delay in our ability to effectively execute our current business strategy and to implement new strategies.Anti- takeover provisions under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.Because we are incorporated in Delaware,we are governed by the provisions of Section 203 of the Delaware General Corporate Law,which prohibits stockholders owning in excess of 15 % of our outstanding voting stock from merging or combining with us.Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors,they would apply even if the offer may be considered beneficial by some stockholders.In addition,these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors,which is responsible for appointing the members of management.Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders,which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors,officers or other employees.Our bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf,any action asserting a breach of fiduciary duty owed by any of our directors,officers or other employees to us or our stockholders,any action asserting a claim against us arising pursuant to any provisions of the Delaware General Corporation Law,our certificate of incorporation or our bylaws,or any action asserting a claim against us that is governed by the internal affairs doctrine.The choice of forum provision may limit a stockholder' s ability **to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors,officers or other employees,which may discourage such lawsuits against us and our directors,officers and other employees.If a court were to find the choice of forum provision contained in the bylaws to be inapplicable or unenforceable in an action,we may incur additional costs associated with resolving such action in other jurisdictions** Failure to maintain effective internal control over financial reporting could have a material adverse effect on our reputation, results of operations and financial condition. Effective internal control over financial reporting is necessary for us to provide reliable financial reports, prevent fraud and operate successfully as a public company. Any failure to execute on our internal controls and continue to maintain effective internal controls, to timely implement any necessary additional improvement to our internal controls or to effect remediation of any future material weakness or significant deficiency could, among other things, result in losses from fraud or error, harm our reputation or cause investors to lose confidence in our reported financial information, all of which could have a material adverse effect on our reputation, results of operations, or financial condition. Management reviews and updates our systems of internal controls and procedures, as appropriate. Any system of controls is based in part on certain assumptions and can provide only reasonable, not absolute, assurances that the objectives of the system are met. Any failure or circumvention of our controls and procedures or failure to comply with regulations related to controls and procedures could have a material adverse effect on our reputation, results of operations and financial condition. Because our merger resulted in an ownership change under Section 382 of the U.S.Internal Revenue Code for OncoGenex,pre- merger net operating loss carryforwards and certain other tax attributes are now subject to limitations.If a corporation undergoes an " ownership change " within the meaning of Section 382 of the U.S.Internal Revenue Code,the corporation' s net operating loss carryforwards and certain other tax attributes arising from before the ownership change are subject to limitations on use after the ownership change.In general,an ownership change occurs if there is a cumulative change in the corporation' s equity ownership by certain stockholders that exceeds fifty percentage points over a rolling three- year period.Similar rules may apply under state tax laws.Our 2017 merger involving OncoGenex and Achieve Life Sciences,Inc.resulted in an ownership change for OncoGenex and,accordingly,OncoGenex' s net operating loss carryforwards and certain other tax attributes will be subject to limitations on their use after the merger.Additional ownership changes in the future could result in additional limitations on the combined organization' s net operating loss carryforwards.Consequently,even if we achieve profitability,we may not be able to utilize a material portion of our net operating loss carryforwards and other tax attributes,which could have a material adverse effect on cash flow and results of operations. U. S. federal tax reform and changes in other tax laws could increase our tax burden and adversely affect our business and financial condition. In December 2017, the U. S. government enacted comprehensive tax legislation, the Tax Cuts and Jobs Act of 2017, significantly reforming the Internal Revenue Code of 1986, as amended. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense, (iii) a shift of the U. S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U. S. income tax base) and (iv) a one-

time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate. In addition, beginning in 2022, tax legislation requires research and experimental expenditures to be capitalized and amortized ratably over a five- year period. Any such expenditures attributable to research conducted outside the United States must be capitalized and amortized over a 15- year period. Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. Furthermore, it is uncertain if and to what extent various states will conform to the enacted federal tax law or any newly enacted federal legislation. In addition, new legislation or regulation which could affect our tax burden **, or that of our suppliers,** could be enacted by any governmental authority **, including foreign tax authorities** . We cannot predict the timing or extent of such tax ‑related developments which could have a negative impact on our financial results. Additionally, we use our best judgment in attempting to quantify and reserve for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax ‑related assumptions could have a material adverse effect on our business, results of operations, or financial condition.