



NEWS RELEASE

Savara Initiates Phase 2a Clinical Study of Molgradex for the Treatment of NTM Lung Infection

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AUSTIN, TX -- (Marketwired) -- 03/13/18 -- **Savara Inc.** (NASDAQ: SVRA), an orphan lung disease company, announced today the initiation of a Phase 2a clinical study, **OPTIMA**, evaluating its lead product candidate Molgradex, an inhaled formulation of recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of nontuberculous mycobacterial (NTM) lung infection. Molgradex is also currently being investigated in a global pivotal Phase 3 clinical study, **IMPALA**, for the treatment of autoimmune pulmonary alveolar proteinosis (PAP).

"The initiation of the OPTIMA study is a major milestone for Savara as we begin to explore the potential of Molgradex as a novel therapeutic approach for NTM infection," stated Rob Neville, chief executive officer of Savara. "We believe that Molgradex may significantly improve patient outcomes by stimulating the innate immune system in the lungs, as compared with targeting bacteria directly, thereby avoiding problems of antibiotic resistance and antibiotic intolerance. We believe Molgradex will be eligible for Orphan Status as well as Qualified Infectious Disease Product Status, and if the results of the OPTIMA study meet our expectations, the product may also qualify for Breakthrough Therapy Designation."

NTM lung infection is a considerable therapeutic challenge due to the unique ability of these bacteria to evade the normal killing mechanisms of alveolar macrophages, a type of immune cell responsible for defending against bacteria in the lungs. Scientific research in various animal models, including GM-CSF knock out mice, have demonstrated that GM-CSF plays an important role as an effector molecule activating macrophages to kill mycobacteria, with or without the simultaneous use of antibiotics. Among the various NTM species, *Mycobacterium abscessus* (*M. abscessus*) is a particularly challenging clinical problem, being one of the most resistant organisms to antibiotics.



Notably, two clinical case reports exploring the use of aerosolized GM-CSF for the treatment of *M. abscessus* were recently published in the **European Respiratory Journal** by Mark E. Wylam, M.D., Pulmonologist and Critical Care Specialist at the **Mayo Clinic College of Medicine**, and his coworkers. In these two cases, both involving individuals living with cystic fibrosis (CF), inhaled GM-CSF either eradicated or dramatically reduced *M. abscessus* infection, improved clinical outcome, and was well tolerated.

"Treatment of NTM lung infection with long multi-drug antibiotic regimens is challenging, places significant burden on patients, and yet frequently fails to eradicate the infection," stated Rachel Thomson, M.B.B.S., Ph.D., Thoracic Physician, Associate Professor, The University of Queensland, Australia and one of the coordinating investigators on the OPTIMA study. "Based on the emerging scientific rationale and the encouraging outcomes of the first clinical cases treated with inhaled GM-CSF, I believe Molgradex represents a promising novel approach into this disease desperate for more effective treatment options."

About the OPTIMA Phase 2a Clinical Study

OPTIMA is an open-label, non-controlled, multi-center, Phase 2a clinical study of Molgradex in 30 subjects (≥ 18 years of age) with persistent pulmonary NTM infection. OPTIMA will enroll subjects with chronic *M. abscessus* or *Mycobacterium avium* complex (MAC) infection, with all subjects having either antibiotic refractory infection or intolerance to standard NTM antibiotics. Subjects with CF will not be enrolled. The study will comprise a 24-week treatment period and a 12-week follow up period. Two subgroups of subjects will be recruited into the OPTIMA study. Group 1 will consist of subjects who remain sputum culture positive while currently on a multidrug NTM guideline based anti-mycobacterial regimen, which has been ongoing for at least six months prior to the baseline visit. Group 2 will consist of subjects who remain sputum culture positive, but have either stopped a multidrug NTM guideline based anti-mycobacterial regimen at least 28 days prior to screening due to lack of response or intolerance, or never started such treatment.

The primary endpoint will be sputum culture conversion, defined as at least three consecutive sputum samples without growth of NTM. Secondary endpoints include: (i) the number of subjects with sputum smear conversion to negative, defined as at least three consecutive negative acid-fast bacilli (AFB) stained sputum smears on microscopy among subjects who were smear positive at baseline, (ii) the number of subjects with durable sputum culture conversion, defined as sputum culture conversion at or before week 24 and culture still negative for growth of NTM at 12-week follow up, (iii) the number of subjects with durable sputum smear conversion, defined as sputum smear conversion at or before week 24 and AFB stained smear still negative for NTM at 12-week follow up among subjects who were smear positive at baseline, and (iv) other microbiological indicators, exercise capacities and patient reported outcomes.

About NTM Lung Infection

NTM lung infection is a rare and serious lung disorder associated with increased rates of morbidity and mortality. Nontuberculous mycobacteria are naturally-occurring organisms and NTM lung infection can occur when an individual inhales the organism from their environment and develops a slowly progressive and destructive lung disease. NTM lung infection is typically characterized by cough, fatigue and weight loss. NTM infection often becomes chronic and requires long courses of multiple antibiotics, and despite the aggressive treatment regimens, treatment failure rates are high, and recurrence of infection common. Chronic NTM lung infection can have a significant impact on quality of life. There are approximately 50,000 to 80,000 individuals affected by NTM lung infection in the U.S., the most common types involving MAC and *M. abscessus*. There have been few advancements in new systemic treatments for NTM lung infection. However, in a recent Phase 3 clinical study by Insmed, local delivery of an inhaled form of amikacin directly to the lung was shown to be effective in approximately one third of treatment refractory patients with pulmonary MAC infection, suggesting administration of high local concentrations of drug directly at the site of infection provides an attractive new avenue to improve clinical outcomes in this and other difficult-to-treat chronic lung infections.

About Molgradex

Molgradex is an inhaled formulation of recombinant human GM-CSF, in Phase 3 development for PAP and in Phase 2a development for nontuberculous mycobacteria, or NTM, lung infection. Molgradex is delivered via an investigational eFlow® Nebulizer System (PARI Pharma GmbH). Molgradex has been granted Orphan Drug Designation for the treatment of PAP in the United States and the European Union.

About Savara

Savara Inc. is an orphan lung disease company. Savara's pipeline comprises: Molgradex, an inhaled granulocyte-macrophage colony-stimulating factor, or GM-CSF, in Phase 3 development for PAP, and in Phase 2a development for NTM lung infection; and AeroVanc, a Phase 3 stage inhaled vancomycin for treatment of MRSA infection in cystic fibrosis. Savara's strategy involves expanding its pipeline of potentially best-in-class products through indication expansion, strategic development partnerships and product acquisitions, with the goal of becoming a leading company in its field. Savara's management team has significant experience in orphan drug development and pulmonary medicine, in identifying unmet needs, developing and acquiring new product candidates, and effectively advancing them to approvals and commercialization. More information can be found at www.savarapharma.com. (Twitter: [@SavaraPharma](https://twitter.com/SavaraPharma))

Forward-Looking Statements

Savara cautions you that statements in this press release that are not a description of historical fact are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by the use of words referencing future events or circumstances such as "expect," "intend," "plan," "anticipate," "believe," and "will," among others. Such statements include, but are not limited to,



statements relating to the initiation of the OPTIMA study being a major milestone for Savara, our belief that Molgradex may significantly improve patient outcomes by stimulating the innate immune system in the lungs, as compared with targeting bacteria directly, thereby avoiding problems of antibiotic resistance and antibiotic intolerance, our belief that Molgradex will be eligible for Orphan Status as well as Qualified Infectious Disease Product Status, that Molgradex may qualify for the breakthrough therapy designation if the results of the OPTIMA study meet our expectations, the belief that based on the emerging scientific rationale and the encouraging outcomes of the first clinical cases treated with GM-CSF, Molgradex represents a promising novel approach to the treatment of NTM, that NTM is desperate for more effective treatment options, that in a recent Phase 3 clinical study by Insmed, local delivery of an inhaled form of amikacin directly to the lung was shown to be effective in approximately one third of treatment refractory patients with pulmonary MAC infection, suggesting administration of high local concentrations of drug directly at the site of infection provides an attractive new avenue to improve clinical outcomes in this and other difficult-to-treat chronic lung infections, and Savara's strategy. Savara may not actually achieve any of the matters referred to in such forward-looking statements, and you should not place undue reliance on these forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon Savara's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with the outcome of our ongoing clinical studies for our product candidates (including our Phase 2a clinical study of Molgradex for the treatment of NTM), the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the availability of sufficient resources for Savara's operations and to conduct or continue planned clinical development programs (including our Phase 2a clinical study of Molgradex for the treatment of NTM), the ability to obtain the necessary patient enrollment for our Molgradex Phase 2a clinical study for the treatment of NTM and for our other product candidates and indications in a timely manner, the timing and ability of Savara to raise additional equity capital to fund continued operations; the ability to successfully develop our product candidates, and the risks associated with the process of developing, obtaining regulatory approval for and commercializing drug candidates such as Molgradex and AeroVanc that are safe and effective for use as human therapeutics. All forward-looking statements are expressly qualified in their entirety by these cautionary statements. For a detailed description of our risks and uncertainties, you are encouraged to review our documents filed with the SEC including our recent filings on Form 8-K, Form 10-K and Form 10-Q. You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date on which they were made. Savara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as may be required by law.

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