



NEWS RELEASE

Savara Reports Publication of Case Reports of Inhaled Granulocyte-Macrophage Colony Stimulating Factor for the Treatment of Nontuberculous Mycobacteria

2018-02-06

AUSTIN, TX -- (Marketwired) -- 02/06/18 -- **Savara Inc.** (NASDAQ: SVRA), an orphan lung disease company, reports the publication of two case reports exploring the use of aerosolized granulocyte-macrophage colony stimulating factor (GM-CSF) for the treatment of *Mycobacterium abscessus* (*M. abscessus*), a species of multidrug-resistant nontuberculous mycobacteria (NTM), in individuals living with Cystic Fibrosis (CF). The case reports, published in the **European Respiratory Journal** (ERJ), authored by clinicians at the **Mayo Clinic College of Medicine**, show inhaled GM-CSF eradicated or dramatically reduced *M. abscessus* infection, improved clinical outcome, and was well tolerated.

"NTM and in particular *M. abscessus* are very difficult to eradicate in patients with chronic lung disease, such as CF, and seriously affect patient morbidity," stated Mark E. Wylam, M.D., Pulmonologist and Critical Care Specialist at Mayo Clinic, Rochester, MN, and senior author of the ERJ publication. "Having successfully pioneered inhaled GM-CSF for over a decade in patients with pulmonary alveolar proteinosis (PAP), we were prompted to try the same approach to treat NTM infection after learning of the increasing scientific evidence of GM-CSF's important role in activating macrophages to kill mycobacteria. Both of our patients had a long history of *M. abscessus* infection that we had not been successful in treating, and both were experiencing a decline in their clinical condition, but when started on inhaled GM-CSF treatment, both demonstrated rapid microbiological response and clinical improvement."

"We believe the Mayo Clinic case reports strongly reinforce the scientific rationale for treatment of NTM lung infection using Molgradex, our proprietary inhaled form of GM-CSF, and we are excited to be initiating our Phase 2a study of Molgradex in NTM infection later this quarter," stated Rob Neville, Chief Executive Officer of Savara.



"Molgradex offers a novel treatment approach for NTM infection by stimulating the human immune system in the lungs with localized delivery of GM-CSF, directly into the site of infection. Whereas Molgradex may be effective on its own against NTM infection, we envision it may also be useful in combination with any of the current or future antibiotic regimens. Furthermore, if Molgradex proves to be effective against NTM infection, such effectiveness could open up a whole new avenue to study Molgradex for the treatment of other chronic lung infections associated with deficiency of the innate immune system."

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 killing 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, *M. abscessus* is a particularly challenging clinical problem, being one of the most resistant organisms to antibiotics. Resistance to antibiotics in general is an increasing problem globally, but importantly, GM-CSF is not an antibiotic. Instead, it stimulates the human immune response without targeting the bacteria directly, thus avoiding the problem of inducing antibiotic resistance. The two published clinical case reports suggest that the promising animal data on the antimycobacterial efficacy of GM-CSF may be translatable to humans, and that GM-CSF may enable eradication or reduction of the bacterial burden in patients with refractory *M. abscessus* or other NTM lung infection.

Savara is currently preparing to initiate a 30-patient, multi-center, open-label Phase 2a clinical trial to investigate the efficacy and safety of Molgradex for the treatment of chronic NTM lung infection. Subjects with either *M. abscessus* or *Mycobacterium avium* complex (MAC) infection will be enrolled, with all subjects having either antibiotic refractory infection or intolerance to standard NTM antibiotics. Subjects with CF will not be enrolled. The trial will consist of 24 weeks of Molgradex treatment, followed by a 12-week observational period. The primary endpoint will be sputum culture conversion defined as at least three consecutive negative sputum cultures. Secondary endpoints include other microbiological indicators, exercise capacity, 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 trial by Insmid, 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 preparation for 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 a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel therapies for the treatment of serious or life-threatening rare respiratory diseases. Savara's pipeline comprises: Molgradex, an inhaled granulocyte-macrophage colony-stimulating factor, or GM-CSF, in Phase 3 development for PAP, and in preparation for Phase 2a development for NTM lung infection; AeroVanc, a Phase 3 stage inhaled vancomycin for treatment of MRSA infection in Cystic Fibrosis; and, Aironite, an inhaled sodium nitrite for heart failure with preserved ejection fraction, or HFpEF, in Phase 2 development. 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 increasing scientific evidence of GM-CSF's important role in activating macrophages to kill mycobacteria, our belief that the Mayo Clinic case reports strongly reinforce the scientific rationale for treatment of NTM lung infection using Molgradex, being excited to be initiating our Phase 2a study of Molgradex in NTM infection later this quarter, that Molgradex may be effective on its own against NTM infection, that we envision it may also be useful in combination with any of the current or future antibiotic regimens, that if Molgradex proves to be effective against NTM infection, such effectiveness could open up a whole new avenue to study Molgradex for

the treatment of other chronic lung infections, that resistance to antibiotics in general is an increasing problem globally, that the two published clinical case reports suggest that the promising animal data on the antimycobacterial efficacy of GM-CSF may be translatable to humans, that GM-CSF may enable eradication or reduction of the bacterial burden in patients with refractory NTM infection, that Savara is currently preparing to initiate a 30-patient, multi-center, open-label Phase 2a clinical trial to investigate the efficacy and tolerability of Molgradex, that in a recent Phase 3 clinical trial 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 trials for our product candidates (including the Phase 2a study of Molgradex for 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 study of Molgradex for NTM), the ability to obtain the necessary patient enrollment for our product candidates in a timely manner (including our Phase 2a study of Molgradex for NTM), the ability to successfully develop our product candidates, the risks associated with the process of developing, obtaining regulatory approval for and commercializing drug candidates such as Molgradex, AeroVanc and Aironite that are safe and effective for use as human therapeutics and the timing and ability of Savara to raise additional equity capital as needed to fund continued operations. 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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Source: Savara Inc.