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Matinas BioPharma Successfully Reaches Agreement with FDA for a Single Phase 3 Registration Trial to Support an NDA for MAT2203 for the Treatment of Invasive Aspergillosis

ORALTO Phase 3 trial focused on desired initial target indication of early oral step-down treatment of invasive aspergillosis infections in adults who have limited or no treatment options

Non-inferiority trial will enroll approximately 216 patients with primary endpoint of all-cause mortality at day 42

Key secondary endpoint includes superiority of oral step-down treatment with MAT2203 vs. AmBisome® (liposomal amphotericin B) for treatment-related toxicities leading to changes in treatment

BEDMINSTER, N.J., Feb. 20, 2024 (GLOBE NEWSWIRE) -- Matinas BioPharma (NYSE American: MTNB), a clinical-stage biopharmaceutical company focused on delivering groundbreaking therapies using its lipid nanocrystal (LNC) platform delivery technology, announces alignment with the U.S. Food and Drug Administration (FDA) on the design of a single Phase 3 registration trial of MAT2203 in patients with invasive aspergillosis who have limited treatment options (the "ORALTO" trial).

The ORALTO trial design is built upon the successful Phase 2 EnACT trial that confirmed MAT2203's efficacy and safety as a step-down and all-oral therapy in HIV patients with cryptococcal meningitis, as well as the Company's ongoing Compassionate/Expanded Use Access Program in individuals suffering from severe invasive fungal infections with no other treatment options.

"We are pleased to achieve alignment with the FDA on the design of a single Phase 3 trial to support the registration of MAT2203 for the treatment of invasive aspergillosis in patients with limited treatment options," commented Dr. Theresa Matkovits, Chief Development Officer at Matinas. "We greatly appreciate the opportunity to work collaboratively with the FDA, which was essential for reaching consensus on all critical elements of the registrational path for MAT2203. Importantly, we view ORALTO as a registration trial with a high probability of clinical success given the ongoing positive patient clinical experience in our Compassionate/Expanded Use Access Program, which mirrors the patients to be enrolled in our upcoming Phase 3 registration trial."

“Reaching this agreement with the FDA is a major milestone for Matinas and a testament to the dedication and expertise of our collective team,” added Jerome D. Jabbour, Chief Executive Officer of Matinas. “We are energized by the support and guidance from the FDA, and believe this alignment provides the requisite certainty to advance our partnership discussions for this important product. We are pursuing every opportunity to secure a partner and to advance MAT2203 into this Phase 3 registration trial as quickly as possible.”

About ORALTO

ORALTO is a Phase 3, randomized, multicenter, open-label, adjudicator-blinded study to evaluate the efficacy and safety of MAT2203 as an oral step-down treatment following treatment with AmBisome (liposomal IV-amphotericin B) compared with the standard of care in patients with invasive aspergillosis who have limited treatment options. The primary efficacy endpoint is all-cause mortality at study day 42. Key secondary objectives include:

(a) demonstration of superiority of oral-step down treatment with MAT2203 compared with AmBisome for treatment-related toxicities leading to changes in treatment (i.e., dose adjustment/discontinuations or changes to treatment regimens);

(b) long-term survival benefit of MAT2203 using all-cause mortality at study day 84;

(c) evaluation of the impact of MAT2203 on healthcare resource utilization and quality of life impact.

Enrollment is expected to include approximately 216 adults with recently diagnosed probable or proven invasive aspergillosis who are being treated with AmBisome due to their inability to receive an IV mold-active azole and with limited alternative treatment options. Following up to two days of initial treatment with AmBisome, eligible study participants will be entered into the study and randomized in a 2:1 ratio to receive either oral MAT2203 or continued AmBisome treatment followed by standard of care.

All study participants will receive up to 12 weeks of treatment starting from the first day of treatment with AmBisome. It is anticipated that all study participants will be hospitalized during the initial AmBisome treatment period. After step-down to oral MAT2203, study participants may be discharged from the hospital to continue treatment on an outpatient basis, as clinically appropriate.

An independent Data Review Committee, who will be blinded to treatment, will adjudicate primary and secondary endpoints, including clinical, radiological, and mycological responses. Once approximately 75% of participants are enrolled, an independent Data Safety Monitoring Board will review the overall pooled all-cause mortality rate in a blinded fashion to ensure that the sample size assumptions are reasonable and that the study is adequately powered. Should the pooled event differ substantially from expected levels, a sample size adjustment can be made to the trial.

ORALTO will be a global trial conducted at approximately 65 investigator sites in the U.S., Europe, South America, Middle East, and Asia Pacific. Enrollment is expected to commence in the second half of 2024 and is expected to require approximately 24 months.

About Invasive Aspergillosis in Patients with Limited Treatment Options

Invasive aspergillosis (IA) is a serious and life-threatening invasive fungal infection that occurs primarily in severely immunocompromised patients with hematological malignancies and in transplant recipients. IA has been increasing globally due to advancements in the medical management of these patients and has recently been recognized as a global public health concern. In 2022, the World Health Organization released their Fungal Priority Pathogen List that designated *Aspergillus fumigatus*, the most common cause of IA, to be in the Critical Priority group (i.e., the highest perceived public health threat). *Aspergillus* is also included in the FDA qualified designation list of pathogens that pose a serious and life-threatening risk.

The one-year mortality for patients with IA has been reported to be 41% in solid organ transplant recipients and up to 75% in stem cell transplant recipients. Although outcomes have improved since the development of mold-active azoles, the use of these agents is often complicated by treatment-limiting toxicities, drug-drug interactions, and the recent emergence of drug resistance.

The Infectious Diseases Society of America (IDSA) Treatment Guidelines recommend that patients with IA receive treatment with a mold-active azole for a minimum of 6 to 12 weeks, largely dependent on the degree and duration of immunosuppression, site of disease, and evidence of disease. Although the mold-active azoles are generally effective, their use requires a considerable degree of expertise to manage toxicities and drug-drug interactions which often limit duration of treatment.

IA caused by *Aspergillus* species that are resistant to mold-active azoles has been increasing globally due to the chronic use of azoles and the widespread use of azole fungicides in agriculture. This emerging resistance is particularly concerning because IA due to azole-resistant *Aspergillus* is a life-threatening disease with a high mortality rate.

Patients with hematological malignancies and transplant recipients often receive antifungal prophylaxis with a mold-active azole to prevent infection during high-risk periods. Recently, cases of breakthrough IA have been reported in patients receiving antifungal prophylaxis. The reason for these apparent failures of prophylaxis may be non-compliance, poor absorption, drug-drug interactions, or infection with a drug-resistant *Aspergillus* species.

The IDSA Treatment Guidelines recommend an intravenously administered amphotericin B, such as AmBisome, as an alternative for patients with IA who are unable to receive treatment with a mold-active azole. However, IV amphotericin B can cause nephrotoxicity and electrolyte abnormalities which usually requires hospitalization for close monitoring and electrolyte supplementation. Other complications of IV amphotericin B include acute infusion reactions with dyspnea, hypoxia, chest and back pain, IV-site phlebitis, anemia, and hepatotoxicity. As such, treatment with IV amphotericin B for more than a few weeks is generally not safe or practical. There are no oral antifungals available that will enable these patients to complete the recommended 6 to 12 weeks of treatment. Accordingly, there is a critical unmet medical need for effective and well-tolerated oral antifungal agents to treat these patients with IA.

MAT2203 is not yet licensed or approved anywhere globally.

About MAT2203

Matinas BioPharma is developing MAT2203 as a potential oral broad-spectrum treatment for

invasive deadly fungal infections. Although amphotericin B is a fungicidal agent, it is currently only available through an intravenous route of administration, which is known to be associated with several significant safety issues such as renal toxicity and anemia due to very high circulating levels of amphotericin B. MAT2203 has the potential to overcome the significant limitations of the currently available amphotericin B products due to its targeted oral delivery, combining comparable fungicidal activity with targeted delivery resulting in a lower risk of toxicity and potentially creating the ideal antifungal agent for the treatment of invasive fungal infections. MAT2203 was successfully evaluated in the completed Phase 2 EnACT study in cryptococcal meningitis, meeting its primary endpoint and achieving robust survival.

About Matinas BioPharma
Matinas BioPharma is a biopharmaceutical company focused on delivering groundbreaking therapies using its lipid nanocrystal (LNC) platform delivery technology.

In addition to MAT2203, preclinical and clinical data have demonstrated that this novel technology can potentially provide solutions to many challenges of achieving safe and effective intracellular delivery of both small molecules and larger, more complex molecular cargos including small oligonucleotides such as ASOs and siRNA. The combination of its unique mechanism of action and flexibility with routes of administration (including oral) positions Matinas' LNC technology to potentially become a preferred next-generation orally available intracellular drug delivery platform. For more information, please visit www.matinasbiopharma.com.

Forward-looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including those relating to our business activities, our strategy and plans, the future development of its product candidates, including MAT2203, the Company's ability to identify and pursue development, licensing and partnership opportunities for its products, including MAT2203, or platform delivery technology on favorable terms, if at all, and the ability to obtain required regulatory approval and other statements that are predictive in nature, that depend upon or refer to future events or conditions. All statements other than statements of historical fact are statements that could be forward-looking statements. Forward-looking statements include words such as "expects," "anticipates," "intends," "plans," "could," "believes," "estimates" and similar expressions. These statements involve known and unknown risks, uncertainties and other factors which may cause actual results to be materially different from any future results expressed or implied by the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to, our ability to continue as a going concern, our ability to obtain additional capital to meet our liquidity needs on acceptable terms, or at all, including the additional capital which will be necessary to complete the clinical trials of our product candidates; our ability to successfully complete research and further development and commercialization of our product candidates; the uncertainties inherent in clinical testing; the timing, cost and uncertainty of obtaining regulatory approvals; our ability to protect the Company's intellectual property; the loss of any executive officers or key personnel or consultants; competition; changes in the regulatory landscape or the imposition of regulations that affect the Company's products; and the other factors listed under "Risk Factors" in our filings with the SEC, including Forms 10-K, 10-Q and 8-K. Investors are cautioned not to place undue reliance on such forward-

looking statements, which speak only as of the date of this release. Except as may be required by law, the Company does not undertake any obligation to release publicly any revisions to such forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. Matinas BioPharma's product candidates are all in a development stage and are not available for sale or use.

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Source: Matinas BioPharma Holdings, Inc.