October 21, 2022

Matinas BioPharma Announces Positive Interim Data from the Phase 2 EnACT Trial of MAT2203 for the Treatment of Cryptococcal Meningitis, Exceeding Primary Endpoint Threshold; Patient Survival in All-Oral Cohort 4 Regimen Currently 90%

Two-week survival in Cohort 4 (all-oral regimen) was 95% in 40 patients receiving MAT2203

Mean Early Fungicidal Activity (EFA) of the rate of yeast clearance in cerebrospinal fluid exceeded the prespecified primary endpoint threshold of >0.20 CFU/mL, CSF/day

Favorable safety and tolerability data support longer-term use of MAT2203 with no evidence of kidney toxicity seen with 6 weeks of oral MAT2203 treatment

Overall survival data from Cohorts 2 and 4 of EnACT trial (Cohorts 1 and 3 were safety lead-ins) provide clinically meaningful evidence of the safety and efficacy of MAT2203 for both a step-down indication and an all-oral treatment regimen for cryptococcal meningitis

Phase 3 registration trial of MAT2203 for treatment of cryptococcal meningitis to commence Q1 2023

BEDMINSTER, N.J., Oct. 21, 2022 (GLOBE NEWSWIRE) -- Matinas BioPharma Holdings, Inc. (NYSE AMER: MTNB), a clinical-stage biopharmaceutical company focused on improving the intracellular delivery of nucleic acids and small molecules with its lipid nanocrystal (LNC) platform delivery technology, today announced positive interim data from Cohort 4, the fourth and final cohort of the Phase 2 EnACT trial evaluating MAT2203, an oral LNC formulation of amphotericin B, for the treatment of cryptococcal meningitis.

Interim EnACT Cohort 4 data from 40 MAT2203 treatment arm participants and 40 standard of care (SOC) controls will be presented today by Drs. Mucunguzi Atukunda, MBChB, MPH of the Infectious Diseases Institute of Makarere University in Uganda and David Boulware, MD, MPH of the University of Minnesota Medical School during the IDWeek 2022 conference, currently taking place in Washington DC. Importantly, Cohort 4 (an all-oral treatment regimen with MAT2203) met its prespecified primary endpoint, exceeding the target rate of CSF yeast clearance threshold of >0.20 colony forming units (CFUs) per mL of

cerebrospinal fluid per day. Overall survival in Cohort 4, a key secondary endpoint of the study, is 95 % at two weeks and currently 90% overall, with ongoing final follow-up through 18 weeks. Matinas plans to initiate the Phase 3 registration trial of MAT2203 as step-down therapy in cryptococcal meningitis in the first quarter of 2023.

“A positive Phase 2 study for any drug is a major milestone for a biotech company. We would first like to thank all of the EnACT patients, our dedicated investigators and the entire clinical study staff in Uganda for their commitment to this important clinical trial,” commented Jerome D. Jabbour, Chief Executive Officer of Matinas. “MAT2203 performed extremely well in EnACT, with an unprecedented 90% survival of patients in Cohorts 2 and 4. The survival rates seen throughout this trial provide tremendous enthusiasm and confidence as we head into our Phase 3 program, which stands to benefit from a flexible, FDA-reviewed design which we believe significantly de-risks this later stage clinical program. In looking beyond the immediate success with MAT2203, these data also represent significant clinical validation of our LNC drug delivery platform, with its unique ability to package and deliver a variety of complex molecules in an oral, safe and targeted manner. We’re very excited by the potential for our proprietary LNC technology to play a meaningful role in overcoming significant drug delivery challenges across therapeutic categories.”

EnACT Cohort 4

Cohort 4 of EnACT evaluated the safety and efficacy of an all-oral regimen of MAT2203 (administered with adjunctive flucytosine) for the initial 14-day induction period, with MAT2203 treatment continued for an additional four weeks into the consolidation phase, administered in combination with 800 mg/day of fluconazole. The primary endpoint of EnACT was early fungicidal activity, a direct measurement of the quantitative rate of antifungal activity at the site of infection in the cerebrospinal fluid (CSF) surrounding the brain, a well-recognized key surrogate marker for survival. The pre-specified target threshold of 0.20 in EnACT is clinically meaningful and represents a robust degree of fungal clearance that is associated with enhanced survival. Treatment early fungicidal activity beyond the >0.20 threshold have not resulted in any observed incremental benefit.[1] Cohort 4 also included secondary endpoints of overall survival, prevention of relapse, CSF sterilization, and safety.

“The Phase 2 clinical trial data to be presented today at IDWeek, testing oral MAT2203 with flucytosine for the treatment of cryptococcal meningitis, are quite exciting, with an approximately 90% survival through 18 weeks. These interim results potentially open other opportunities to explore this oral amphotericin therapy for other difficult to treat or resistant invasive fungal infections.” said David R. Boulware, M.D., MPH, Professor of Medicine, University of Minnesota Medical School, and co-principal investigator of the EnACT Trial. “One of the most important findings was reduced toxicity. With 6 weeks of oral LNC-enabled oral amphotericin B, statistically fewer lab abnormalities occurred than with 1 week of intravenous amphotericin B.”

Interim Results from Cohort 4

The key interim results from Cohort 4 of EnACT include exceeding the prespecified early fungicidal activity threshold of >0.20 CFU/mL CSF/day, survival, and the safety of longer-term use of an oral formulation of amphotericin B (MAT2203) for up to 6 weeks.

Exceeding Key Early Fungicidal Activity Threshold

- In Cohort 4, the CSF yeast clearance rate exceeded the prespecified primary endpoint threshold target of >0.20, with a mean early fungicidal activity achieved of 0.30 $\log_{10}$ CFU/mL/day with 95% confidence intervals from 0.22 – 0.38.

- Several participants with high baseline fungal burdens had noteworthy antifungal activity within the MAT2203 treatment arm, including one patient with quantitative cryptococcal culture as high as 915,000 CFU/mL at the time of screening with effective clearance during the induction period, a key demonstration of potent antifungal activity, even in the most challenging of cases.

Survival

- In Cohort 4, in 40 patients receiving MAT2203 treatment, interim survival is currently 90%, while the survival rate at Week 2 was 95%; note that Week 2 survival is the prespecified primary endpoint for the MAT2203 Phase 3 registration trial in cryptococcal meningitis.

Safety

- MAT2203 patients had fewer Grade ≥3 Clinical adverse events (AEs) (42%) vs. SOC treatment (59%).

- Importantly, the incidence of adverse events relating to kidney function and anemia were significantly lower for MAT2203 compared with the SOC treatment, with no evidence of kidney toxicity seen with 6 weeks of oral MAT2203 treatment.

- The favorable safety and tolerability data seen in Cohort 4 support the use of oral MAT2203 for longer-term use, something not previously feasible due to associated toxicities with currently available IV formulations of amphotericin B.

“Based on these data, we have succeeded in establishing a well-tolerated, all-oral dose regimen for the treatment of cryptococcal meningitis that improves survival in an otherwise devastatingly fatal disease,” commented Dr. Theresa Matkovits, Chief Development Officer of Matinas. “As we move into our Phase 3 registration trial, EnACT Cohort 4 data also provide very favorable 2-week survival data, an added level of confidence as they replicate what we saw in Cohort 2. In addition, we hope to leverage these data from EnACT to further the development of MAT2203 and secure multiple orphan indications for the treatment of other life-threatening invasive fungal infections, such as mucormycosis and aspergillosis, which also require longer-term antifungal treatment.”

Upcoming Phase 3 Trial of MAT2203 in Cryptococcal Meningitis

The pivotal Phase 3 registration trial of MAT2203 in cryptococcal meningitis will be initiated early in the first quarter of 2023 and will assess MAT2203 as step-down therapy after only 2 loading doses of IV amphotericin B (similar to EnACT Cohort 2), building upon the impressive results already documented in EnACT Phase 2 trial. This open-label randomized trial, which will be partially financially supported by the National Institutes of Health (NIH) National Institute of Neurological Disorders and Stroke (NINDS), involves a three arm non-

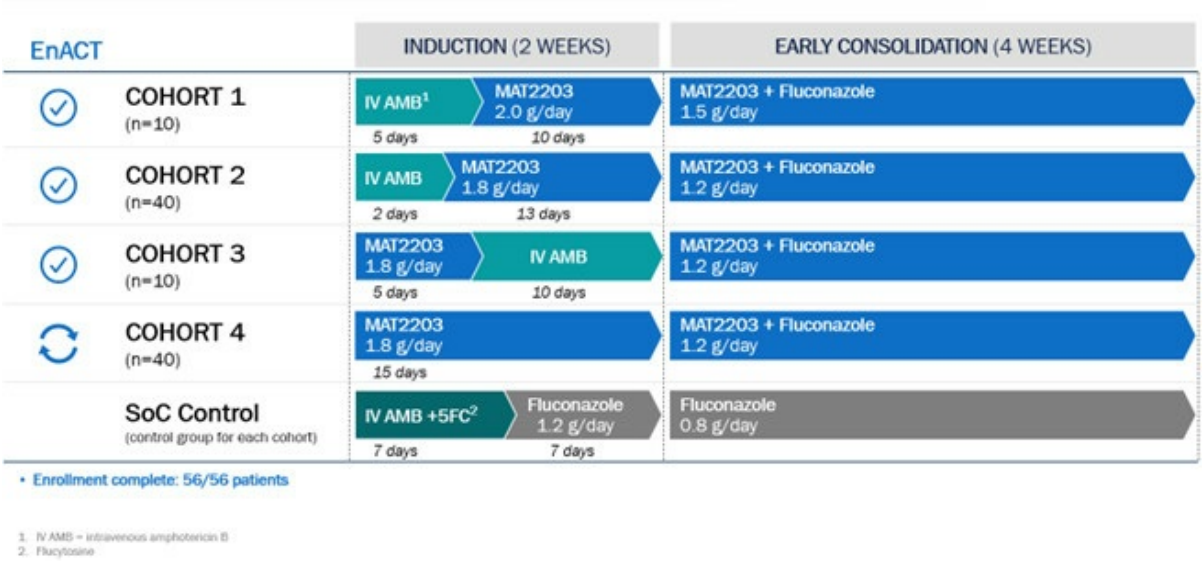
inferiority design in persons living with HIV who have cryptococcal meningitis: (A) step-down therapy with MAT2203 with treatment continuing for 2 weeks; (B) step-down therapy with MAT2203 with treatment out to 6 weeks; and (C) SOC control arm of IV amphotericin induction transitioning to fluconazole. The non-inferiority margin for both the primary and key secondary endpoints will be 10% and total enrollment is planned to be approximately 270 patients, with an adaptive, de-risking design allowing for the potential for additional patients once enrollment has reached 75%. The primary endpoint will be 2-week all-cause mortality, with a pooled analysis across the two MAT2203 treatment arms compared with SOC control to support a potential indication for the treatment of cryptococcal meningitis. To evaluate opportunities to improve survival by extending MAT2203 therapy, a key secondary endpoint is 10-week relapse free survival of optimized treatment (2-weeks or 6-weeks) against SOC will be evaluated for non-inferiority. Selection of the optimal treatment regimen will be based on predefined and protocolized clinical criteria and will then form the basis for a final NDA submission. Following substantial collaboration with the U.S. Food and Drug Administration (FDA) and written feedback from the European Medicines Agency (EMA) in the form of Scientific Advice, as well as external NIH peer-review, the planned Phase 3 study design, including endpoints, is well-positioned to potentially support registration of MAT2203 in both the US and Europe.

FDA has designated MAT2203 as a Qualified Infectious Disease Product (QIDP) with Fast Track status for four indications, specifically, the prevention of invasive fungal infections due to immunosuppressive therapy, and the treatment of invasive candidiasis, invasive aspergillus and cryptococcal meningitis. In addition, the FDA and EMA have granted orphan drug designation to MAT2203 for the treatment of cryptococcosis. If approved, MAT2203 would be eligible for up to 12 years of regulatory exclusivity.

About the EnACT Phase 2 Study

EnACT is a Phase 2 prospective, randomized, open-label, sequential cohort study, financially supported by the NIH NINDS, evaluating the safety, tolerability, and efficacy of MAT2203 in 100 HIV-positive persons with cryptococcal meningitis. MAT2203 utilizes the Company's LNC platform delivery technology to orally deliver the traditionally IV-only fungicidal drug, amphotericin B.

The EnACT trial includes a total of four cohorts of patients, with the first two cohorts testing MAT2203 as early step-down therapy following initial treatment with IV amphotericin B during the induction period, and the second two cohorts testing MAT2203 as potentially all oral therapy. Cohorts 1 and 3 were safety lead-ins to Cohorts 2 and 4, respectively. The induction period for all patients in each cohort (active or control) is 14 days, followed by an additional four weeks of treatment (active or control) during a consolidation/maintenance period.



About Matinas BioPharma

Matinas BioPharma is a biopharmaceutical company focused on improving the intracellular delivery of nucleic acids and small molecules with its lipid nanocrystal (LNC) platform technology. The Company is developing its own internal portfolio of products as well as partnering with leading pharmaceutical companies to develop novel formulations that capitalize on the unique characteristics of the LNC platform.

Preclinical and clinical data have demonstrated that this novel technology can provide solutions to many of the challenges in achieving safe and effective intracellular delivery, for both small molecules and larger, more complex molecules, such as mRNA, DNA plasmids, antisense oligonucleotides, and vaccines. The combination of a unique mechanism of action and flexibility with formulation and route of administration (including oral), positions Matinas' LNC technology to potentially become the preferred next-generation intracellular drug delivery vehicle with distinct advantages over both lipid nanoparticles and viral vectors.

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, our collaboration with BioNTech, the potential of our LNC platform delivery technology, and the future development of its product candidates, including MAT2203, MAT2501, the anticipated timing of regulatory submissions, the anticipated timing of clinical studies, the anticipated timing of regulatory interactions, the Company's ability to identify and pursue development and partnership opportunities for its products 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

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.

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[1] **Clin Infect Dis.** 2020; 71(5):e45-49

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/04396cd4-9bc0-4b53-9f49-086b6d27dcef

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Study Design

EnACT Phase 2 Design