Chiasma Announces Positive Topline Results from the MPOWERED™ Phase 3 Clinical Trial Comparing MYCAPSSA® (octreotide capsules) to Long Acting Injectables for the Maintenance Treatment of Adults with Acromegaly

November 18, 2020

91% of patients on MYCAPSSA maintained IGF-1 response in the 9-month randomized, controlled phase of the non-inferiority trial

Company intends to submit a marketing application for MYCAPSSA in the EU in mid-2021

Company to host conference call today at 8:00 a.m. ET

NEEDHAM, Mass., Nov. 18, 2020 (GLOBE NEWSWIRE) -- Chiasma, Inc. (NASDAQ: CHMA), a commercial-stage biopharmaceutical company utilizing its delivery platform technology to develop and commercialize oral therapies to improve the lives of patients with rare diseases on burdensome and painful injections, today announced positive top-line data from its global Phase 3 MPOWERED™ non-inferiority clinical trial comparing MYCAPSSA® (oral octreotide capsules) to long-acting injectable somatostatin analogs (SSAs) for maintenance of biochemical response in patients with acromegaly. The MPOWERED trial was designed to support a planned marketing authorization application for MYCAPSSA in the European Union. MYCAPSSA is currently approved in the United States for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with injectable octreotide or lanreotide.

The MPOWERED non-inferiority trial was designed to compare long-term maintenance treatment with MYCAPSSA, the first and only approved oral SSA therapy for acromegaly, to the long-acting injectables octreotide long-acting release and lanreotide autogel, in patients previously responding to these therapies. After a six-month run-in phase, 92 patients who were responders to MYCAPSSA were randomized to a nine-month controlled phase with continued treatment on MYCAPSSA or on their prior injectable therapy.

Key Results:

- **The study met its primary non-inferiority endpoint. 91% of patients on MYCAPSSA maintained insulin-like growth factor 1 (IGF-1) response** (95% CI = 80%, 97%) compared to 100% on injectable SSAs (95% CI = 91%, 100%). Response was defined as the time-weighted average of IGF-1 <1.3 x upper limit of normal (ULN) during the 9-month randomized, controlled treatment (RCT) phase.
- **MYCAPSSA maintained mean IGF-1 within normal limits and was comparable to injectable therapy:** mean IGF-1 in the MYCAPSSA cohort at the beginning and end of the RCT phase was 0.9 × ULN and 0.9 × ULN, respectively, compared to 0.8 × ULN and 0.8 × ULN, respectively, in the injectable SSA cohort.

“We are excited with the positive results from the MPOWERED study that demonstrated non-inferiority relative to long-acting SSAs. These results further strengthen the available robust clinical data set for MYCAPSSA and provide additional meaningful information for healthcare providers in treating patients with acromegaly,” said Raj Kannan, chief executive officer of Chiasma. “In light of these positive results, we plan to submit a marketing authorization application for MYCAPSSA to the European Medicines Agency in mid-2021. While we are excited to report the preliminary top line results, further analyses of the trial results are ongoing, and we plan to present the full data set from the study at upcoming medical conferences in 2021.”

“I am pleased that the MPOWERED study met its primary endpoint of non-inferiority compared to long acting SSA injectables. These results should provide treating physicians with confidence that patients on injectables who are switched to oral octreotide can be expected to achieve comparable efficacy and safety,” commented Maria Fleseriu, MD, FACE, lead investigator of the MPOWERED study, Professor of Medicine and Neurological Surgery, Director of the Pituitary Center at Oregon Health and Science University in Portland, Oregon, Immediate Past President of the Pituitary Society. “Many patients with acromegaly experience significant burdens with SSA injections, including injection site pain and reactions, and I believe that the results of the MPOWERED study underscore the importance of an oral treatment alternative for patients with acromegaly.”

MPOWERED ™MYCAPSSA® Safety:

The safety profile of MYCAPSSA capsules in the MPOWERED trial was consistent with the known safety profile of octreotide but without adverse injection site reactions. No new or unexpected safety signals were detected during the study among MYCAPSSA subjects. See Important Safety Information below for contraindications, warnings, precautions and adverse reactions associated with MYCAPSSA based in the current approved labeling in the United States.

Conference Call and Webcast Information

Chiasma management will host a conference call and webcast to discuss the results of the MPOWERED study today, November 18, 2020, at 8:00 a.m. ET. The dial-in number in the U.S. / Canada is 877-407-4018; for international participants, the dial-in number is 201-689-8471. For all callers, please refer to Conference ID 13713200. To access the live webcast, please use the following link: http://public.viavid.com/index.php?id=142448

A live audio webcast of the call may also be accessed under "Events & Presentations" on the News & Investors section of the Company's website, https://ir.chiasma.com/events-presentations. An archived replay of webcast will be available on the Company’s website approximately two hours after the event. The archived webcast will be available for one year.

MPOWERED™ Phase 3 Trial Design

The MPOWERED trial was a global, randomized, open-label and active-controlled, 15-month trial intended to support approval of MYCPASSA in the European Union. Chiasma completed enrollment of 146 adult acromegaly patients into the trial in June 2019, of which 92 patients who were deemed responders to octreotide capsules per the protocol following a six-month run-in were randomized to either octreotide capsules (n=55) or injectable somatostatin receptor ligands (octreotide long-acting release or lanreotide autogel) (n=37), and then followed for an additional nine months. The trial was designed to evaluate the proportion of patients who maintain their biochemical response to octreotide capsules and patient-reported outcomes in patients treated with octreotide capsules, compared to patients treated with leading injectable somatostatin analogs.

About MYCAPSSA
INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE
MYCAPSSA (octreotide) delayed-release capsules, for oral use, is a somatostatin analog indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

CONTRAINDICATIONS
Hypersensitivity to octreotide or any of the components of MYCAPSSA. Anaphylactoid reactions, including anaphylactic shock, have been reported in patients receiving octreotide.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions
MYCAPSSA can cause problems with the gallbladder. Monitor patients periodically. Discontinue if complications of cholelithiasis are suspected.

Blood sugar, thyroid levels, and vitamin B_{12} levels should be monitored and treated accordingly.

Bradycardia, arrhythmia, or conduction abnormalities may occur. Treatment with drugs that have bradycardia effects may need to be adjusted.

ADVERSE REACTIONS
The most common adverse reactions (incidence >10%) are nausea, diarrhea, headache, arthralgia, asthenia, hyperhidrosis, peripheral swelling, blood glucose increased, vomiting, abdominal discomfort, dyspepsia, sinusitis, and osteoarthritis.

DRUG INTERACTIONS
The following drugs require monitoring and possible dose adjustment when used with MYCAPSSA: cyclosporine, insulin, antidiabetic drugs, calcium channel blockers, beta blockers, lisinopril, digoxin, bromocriptine, and drugs mainly metabolized by CYP3A4. Counsel women to use an alternative non-hormonal method of contraception or a back-up method when MYCAPSSA is used with combined oral contraceptives.

Patients taking proton pump inhibitors, H2-receptor antagonists, or antacids concomitantly with MYCAPSSA may require increased dosages of MYCAPSSA.

PREGNANCY
Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, contact the product information department at 1-844-312-2462 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

The full Prescribing Information for MYCAPSSA is available at www.MYCAPSSA.com.

About Acromegaly
Acromegaly typically develops when a benign tumor of the pituitary gland produces too much growth hormone, ultimately leading to significant health problems. Common features of acromegaly are facial changes, intense headaches, joint pain, impaired vision and enlargement of the hands, feet, tongue and internal organs. Serious health conditions associated with the progression of acromegaly include type 2 diabetes, hypertension, respiratory disorders and cardiac and cerebrovascular disease. Chiasma estimates that approximately 8,000 adult acromegaly patients are chronically treated with somatostatin analog injections in the United States.

About Chiasma
Chiasma is a commercial-stage biopharmaceutical company focused on developing and commercializing oral therapies to improve the lives of patients who face challenges associated with their existing treatments for rare and serious chronic diseases. Employing its Transient Permeability Enhancer (TPE®) technology platform, Chiasma seeks to develop oral medications that are currently available only as injections. On June 26, 2020, Chiasma received FDA approval of MYCAPSSA for long-term maintenance therapy in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. MYCAPSSA, the first and only oral somatostatin analog approved by the FDA, is available for commercial sale in the United States. Chiasma is headquartered in Needham, MA with a wholly owned subsidiary in Israel. MYCAPSSA, TPE and CHIASMA are registered trademarks of Chiasma. For more information, please visit the company's website at www.chiasma.com.

Forward-Looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the data from the MPOWERED trial and whether the data will support the submission of a marketing authorization application (MAA) to the European Medicines Agency (EMA) for MYCAPSSA in the European Union and ultimately regulatory approval, statements regarding the timing of an MAA submission and regulatory review, statements regarding the company's plans for the presentation of the full trial results, statements regarding the company's expectations relating to MYCAPSSA for the long-term maintenance therapy in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide, and statements concerning the therapeutic potential of MYCAPSSA, including its ability to become a standard of care. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond the company's control, that may cause actual events or results to differ materially from the company's current expectations. Management's expectations and, therefore, any forward-looking statements in this press release could be affected by risks and uncertainties relating to a number of factors, including the following: the content and timing of decisions made by the EMA, the sufficiency of the data collected from the company's clinical trials to obtain regulatory approval in the European Union or elsewhere, and the impact the ongoing COVID-19 pandemic may have on the company's

business, including its expected development, manufacturing, regulatory and commercialization timelines for MYCAPSSA. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause the company's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Chiasma's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and in subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and the company undertakes no duty to update this information unless required by law.

Investor Relations and Corporate Communications:
Ashley Robinson
LifeSci Advisors, LLC
617-430-7577
arr@lifesciadvisors.com

Media Relations:
Patrick Bursey
LifeSci Communications
646-876-4932
pbursey@lifescicomms.com