Chiasma Presents New Positive Data for MYCAPSSA from Phase 3 Trial MPOWERED™ for the Maintenance Treatment of Acromegaly at ENDO 2021

March 20, 2021

--Data supports MYCAPSSA® as non-inferior to long-acting injectable somatostatin receptor ligands (iSRLs)--

--Data demonstrated patients taking MYCAPSSA had significant improvement in acromegaly related symptoms and patient reported outcomes after switching from iSRLs--

NEEDHAM, Mass., March 20, 2021 (GLOBE NEWSWIRE) -- Chiasma, Inc. (NASDAQ: CHMA), ("Chiasma" or the "Company"), 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 currently treated with burdensome and painful injections, as evidenced by its recent phased launch of MYCAPSSA® as the first oral therapy for the treatment of acromegaly, today announced the presentation of new positive clinical data from its MPOWERED™ Phase 3 trial of MYCAPSSA at the Endocrine Society's annual meeting, ENDO 2021, being held virtually March 20-23, 2021. The data from MPOWERED showed that MYCAPSSA improved clinical symptoms and other patient-reported outcomes compared to long-acting injectable somatostatin receptor ligands (iSRLs) in patients with acromegaly. In addition, MYCAPSSA met the pre-specified non-inferiority margin compared to long-acting iSRLs in maintenance of biochemical response.

"The new encouraging data from all five late-breaking poster presentations further expand our understanding of oral octreotide capsules' potential positive impact for patients with acromegaly who would otherwise need monthly, frequently burdensome SRLs injections," said Maria Fleseriu, M.D., 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, and Immediate Past President of the Pituitary Society. "As a practicing endocrinologist, I believe that these data provide valuable insights to physicians on the potential benefit of a twice daily oral drug versus long-acting injections for most patients."

Raj Kannan, Chief Executive Officer of Chiasma, added, "We are pleased to characterize further the MYCAPSSA product profile with the positive results from Chiasma's MPOWERED study at ENDO 2021 for the medical community. This is the first head-to-head large, non-inferiority Phase 3 trial in acromegaly that has been done to assess safety and efficacy, including the effect on acromegaly symptoms, and on patient satisfaction. Based on these data, we remain focused on submitting a marketing authorization application for MYCAPSSA to the European Medicines Agency planned for mid-2021."

Data highlights from the five late-breaking poster presentations are outlined below:

A Phase 3 Large International Noninferiority Trial (MPOWERED): Assessing Maintenance of Response to Oral Octreotide Capsules In Comparison to Injectable Somatostatin Receptor Ligands

- Data showed that MYCAPSSA demonstrated non-inferiority to iSRLs in maintaining biochemical response, 91% (CI, 80%-97%) of the MYCAPSSA patients maintained insulin-like growth factor 1 (IGF-1) response during the randomized controlled treatment (RCT) phase.
- MYCAPSSA demonstrated stable IGF-1 levels during the RCT phase comparable to iSRLs, supporting efficacy of MYCAPSSA.

Oral Octreotide Capsules Lowered Incidence and Improved Severity of Acromegaly Symptoms Compared to Injectable Somatostatin Receptor Ligands—Results from the MPOWERED Trial

- A statistically significant ($p = 0.001$) reduction from baseline (time of first dose of MYCAPSSA in run-in) was noted in the number of active acromegaly symptoms. Reduction in the number of active symptoms by individual symptom was statistically significant for swelling of extremities ($p = 0.01$) and fatigue ($p = 0.03$).
- The overall mean symptom score decreased from 4.5 to 3.5; the mean change from baseline was statistically significant ($p < 0.001$) and clinically meaningful (> 1 point reduction is equal to a shift of 1 symptom from severe to moderate, or moderate to mild or resolution of 1 symptom).
- Overall, 80.4% of the randomized patients maintained or improved their symptoms score during the run-in phase compared to baseline.
- We believe these findings validate previous results from the open-label, Phase 3 CH-ACM-01 study of MYCAPSSA in which patients switching to MYCAPSSA from iSRLs reported significant reduction in joint pain, extremity swelling and fatigue.

Improved Acromegaly Patient Satisfaction with Oral Octreotide Capsules Compared with Injectable Somatostatin Receptor Ligands in The MPOWERED Trial

- For the 92 patients randomized, 3 of 5 domains (emotional reaction, treatment convenience, and treatment satisfaction) of the Acromegaly Treatment Satisfaction Questionnaire (Acro-TSQ) showed significant improvement at the end of the run-in (n=37) phase (reflecting outcomes on MYCAPSSA) as compared to baseline (reflecting outcomes on iSRLs).

Improvements not reaching statistical significance were also noted for symptom interference and GI interference.

- Patients receiving MYCAPSSA demonstrated a significant improvement in the Acro-TSQ domain of treatment convenience over the RCT phase in comparison to those receiving iSRLs ($p = 0.04$).
- At the end of the RCT phase, breakthrough acromegaly symptoms were reported by 15% of patients in octreotide capsules group and 31% of patients in the iSRLs group.
- Of note, 47% of patients receiving SRL injections during the RCT phase reported injection site reactions via the Acro-TSQ. 81% of these patients reported that iSLRs interfered with their daily activities.

Addition of Cabergoline to Oral Octreotide Capsules May Improve Biochemical Control in Patients with Acromegaly Who Are Inadequately Controlled with Monotherapy

- IGF-1 levels improved in most patients over the 36-week study (n=12; 85.7%).
- Of nine patients with IGF-1 ≥1.3 × ULN at sub-study start, five patients (55.6%; 95% CI, 21.2% -86.3%) exhibited decreases to predefined responder range (<1.3 × ULN) by week 36.
- Adverse event incidence and nature were similar to the known octreotide safety profile and acromegaly disease burden.
- For the first time, a study demonstrated the potential benefit of an all-oral combination treatment for acromegaly with avoidance of injection-related burdens.

Safety Results From MPOWERED, A Phase 3 Trial of Oral Octreotide Capsules in Adults with Acromegaly

- No new or unexpected safety signals were identified during the trial.
- 39 patients (70.9%) in the MYCAPSSA group and 26 (70.3%) in the iSRL group had ≥1 treatment-emergent adverse events (TEAE). Gastrointestinal AEs were the most common TEAEs within both groups.
- Safety results were similar between both groups, but the MYCAPSSA group did not have injection site reactions, whereas 24.3% of patients reported injection site reactions as TEAEs from the iSRL group during the RCT phase.

About the CHIASMA MPOWERED™ Trial

The MPOWERED™ trial was a global, randomized, open-label and active-controlled, 15-month trial intended to support approval of MYCPASSA® (oral octreotide capsules) in the European Union. This non-inferiority clinical trial was designed to compare MYCAPSSA to long-acting injectable somatostatin analogs (SSAs) for maintenance of biochemical response in patients with acromegaly. The trial enrolled 146 adult acromegaly patients of which 92 patients who were responders to MYCAPSSA after a six-month run-in phase were randomized to a nine-month controlled phase with continued treatment on MYCAPSSA or on their prior injectable therapy. Patients were randomized to either MYCAPSSA (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 primary endpoint of the trial was time-weighted average of IGF-1 <1.3 x upper limit of normal (ULN) during the nine-month randomized, controlled treatment (RCT) phase. As previously announced, MPOWERED met its primary endpoint of non-inferiority compared to long acting SSA injectables.

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. In June 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. 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 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 Annual Report on Form 10-K for the year ended December 31, 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 Chiasma undertakes no duty to update this information unless required by law.

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