EMBARGOED UNTIL THURSDAY, MAR. 5 AT 11:30AM PST / 2:30PM EST

Chiasma Announces New Data for Investigational Octreotide Capsules

Two studies presented at ENDO 2015 contribute to growing body of knowledge about acromegaly treatment

Newton, Mass. and Jerusalem, Israel, March 5, 2015 – Chiasma, Inc., a U.S. privately-held biopharma company developing octreotide capsules for the orphan condition acromegaly, today announced two new studies presented at the 97th Endocrine Society (ENDO) Annual Meeting in San Diego, Calif. The studies provide additional data from Chiasma's Phase III trial and new findings on the patient burden of current injection therapies.

"We now have data to help clinicians determine whether octreotide capsules, if approved, are likely to help their patient with acromegaly maintain response," said Shlomo Melmed, M.D., senior vice president and dean, Cedars-Sinai Medical Center, Los Angeles and global study principal investigator. "Furthermore, the Phase III results show the safety and efficacy of octreotide capsules can be reliably determined within 12 weeks of initiating therapy."

"The pain and burden patients with acromegaly endure with intramuscular and deep subcutaneous injections should not be underestimated," said Christian Strasburger, M.D., professor of medicine and chief of clinical endocrinology, Charite Universitatsmedizin, Berlin, Germany. "This study clearly shows the desire for an alternative to injections and the need for consistent symptom control throughout the month."

Chiasma is developing octreotide capsules, an investigational agent for the treatment of acromegaly. Based on Phase III results recently published online by the *Journal of Clinical Endocrinology & Metabolism*, Chiasma intends to submit a New Drug Application to the Food and Drug Administration (FDA) in 2015.

The following data were presented:

Determinants of Oral Octreotide Capsule Efficacy in Acromegaly
Abstract #21142; Oral Session Number: OR09-3
11:30 a.m. to 1:00 p.m. PST

In a multicenter Phase III trial, 151 patients previously managed on injectable somatostatin analogs were switched to the company's investigational octreotide capsules, an oral form of the peptide octreotide, a somatostatin analog, for up to 13 months.

The descriptive analysis studied the relationship between baseline disease activity and the efficacy of octreotide capsules for up to 13 months (study duration). The correlation between prior injection dose and oral octreotide dose was also studied.

Results showed:

- Baseline responses to injectable somatostatin analogs can predict response to oral octreotide. Response rates on octreotide capsules were 76% for patients completely controlled on injections, 44% for patients partially controlled on injections and 24% for patients uncontrolled on injections.

- Previous injectable dose also predicted response; 71% of patients previously treated with mid (or low) doses of injectable somatostatin analogs responded to octreotide capsules; a 49% response rate was observed for patients previously treated with high doses.

- Degree of response was reliably determined within 12 weeks of initiating octreotide capsules and was sustained through the treatment period (up to 13 months) in 85% of patients.

Patient Reported Outcomes (PRO) Survey in Acromegaly Patients Treated with Parenteral Somatostatin Analogs
Abstract #19974; Poster Preview Number: PP09-4
11:15 to 11:30 a.m. PST

A multicenter PRO study of 195 patients across nine endocrinology centers assessed for the first time the impact of chronic injections on the well-being of people with acromegaly. In this observational study, research nurses administered a questionnaire to patients treated with injectable somatostatin analogs.

The survey was fielded among patients diagnosed with acromegaly and managed on somatostatin analogs administered parenterally by intramuscular or deep subcutaneous injections. Of the patients surveyed, 57% received octreotide and 43% received lanreotide, with results showing the injection burden was similar between the two medications.

Results showed:

- 70% of patients reported acromegaly symptoms/signs, with 52% reporting that symptoms became worse toward the end of the dosing interval.

- 70% of patients experienced pain during or after injection, while 36% experienced pain even days later.

- The most frequently reported injection-related symptoms were hardness at injection site (48%), nodules (38%), swelling (28%), bruising (16%) and inflammation (7%).

- 36% of patients felt a loss of independence due to chronic injections.

- 16% of patients regularly miss work for injections (averaging 11 days per year).

- 44% of patients experienced problems with the preparations and administration of the injections.

- Patients expressed a desire for potential future treatment modifications that offer major improvements over current care, including avoiding injections (44%) and better symptom control (41%).

"We believe the studies presented today will help endocrinologists better determine which patients are most likely to maintain control with an oral therapy," said Roni Mamluk, Ph.D., Chiasma's chief executive officer. "If approved, octreotide capsules would be the first and only oral somatostatin analog and would go a long way to serving the needs of people who would prefer an alternative to chronic injections, if available."

About Acromegaly

Acromegaly typically develops when a benign tumor of the pituitary gland produces too much growth hormone (GH), ultimately leading to significant health problems and early death if untreated. Common features of acromegaly are facial changes, intense headaches, joint pain, impaired vision and enlargement of the hands, feet and tongue. Serious associated health conditions include diabetes, hypertension, cardiac and cerebrovascular disease, and respiratory disorders.

Current treatment options include surgery to remove the tumor, radiation therapy which destroys any lingering tumor cells and/or medical treatment in cases where these approaches are not possible or fully effective. Medical treatments available currently include dopamine agonists, GH antagonists and injectable somatostatin analogs, the current standard of care. Currently available somatostatin analogs require large-bore needles, for injections into muscle (octreotide) or deep into the tissue underlying the skin (lanreotide).

Researchers estimate that three to four out of every million people develop acromegaly each year.[1] According to the National Organization for Rare Disorders, acromegaly occurs in approximately 60 people per million in the United States. Because symptoms often develop slowly, diagnosis may be delayed by years or decades, making it difficult to determine the total number of people with the disease.

About Octreotide Capsules

Octreotide capsules are an investigational oral form of the peptide octreotide, a somatostatin analog that is currently available only by injection. Octreotide capsules uses a proprietary technology developed by Chiasma Inc., called Transient Permeability Enhancer (TPE®) that facilitates gastrointestinal absorption of unmodified drug into the bloodstream. Chiasma is independently leading the clinical and regulatory development and commercialization of octreotide capsules for the potential treatment of acromegaly and neuroendocrine tumors.

About Chiasma

Chiasma is a biopharmaceutical company dedicated to improving the lives of patients with rare diseases by developing and commercializing oral medications that were previously available by injection only. The company's lead candidate is octreotide capsules, which has received orphan drug designation from the FDA and EMA. Chiasma is evaluating additional proteins, peptides and small molecule drugs that that are currently only available by injection but could potentially be converted to oral delivery using the company's TPE® technology. Chiasma is a Delaware corporation with a wholly owned Israeli subsidiary.

Additional information can be found at www.ChiasmaPharma.com.

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[1] National Endocrine and Metabolic Diseases Information Service (NEMDIS); A service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)