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Chiasma Reports Successful Oral Delivery Of A Peptide In Clinical Study

On Track To Initiate Pivotal Trial Of Octreolin™ (An Oral Form Of Octreotide Acetate) In Patients With Acromegaly By Year End 2010

New York and Jerusalem, Israel, June 14, 2010. Chiasma, Inc., a privately held biopharma company, announced that it has successfully completed a Phase I clinical study evaluating the safety and pharmacokinetics (PK) of its proprietary product Octreolin, which contains the active ingredient octreotide acetate and is administered orally. Octreolin demonstrated a PK profile similar to that of subcutaneously injected octreotide acetate. In addition, no serious adverse safety events were reported for Octreolin.

The Company also announced that it was advancing towards its goal of beginning a pivotal trial by the end of the year for Octreolin in acromegaly, a hormonal disorder that results from an excess of growth hormone (GH).

Chiasma has submitted an Orphan Drug application to the US FDA for acromegaly and will submit an application for Orphan Medicinal Product Designation to the European Agency for the Evaluation of Medicinal Products (EMA) shortly. The Company intends to file an NDA using the 505(b)(2) regulatory pathway in the US and its EMA equivalent, the Hybrid Application, in Europe.

Information on the Octreolin Trial

The Phase I trial was conducted in 12 healthy volunteers with a cross-over design in which subjects were each administered three single oral doses of Octreolin and a

single subcutaneous injection of octreotide acetate as the reference drug (Sandostatin®). The primary objectives of the trial were to evaluate the safety, tolerability and PK of the three oral doses of Octreolin in comparison to the subcutaneous injection of octreotide acetate. Key findings included:

- No serious adverse events among the Octreolin-treated subjects
- Octreolin was well tolerated by all subjects
- Measurable drug levels were noted in all subjects at all 3 doses of Octreolin
- Linear ratio between Octreolin doses and exposure (AUC) was established
- Drug levels and PK profiles were comparable between Octreolin and the injected reference drug
- Similar elimination half life ($T_{1/2}$) of octreotide regardless of route of administration or dose
- Significant octreotide absorption within the first 40 minutes from capsule administration in all subjects for all 3 doses

Therapeutically relevant blood levels of octreotide, known to induce maximal inhibition of GH in acromegaly patients, were achieved and were maintained for a longer time with Octreolin than after Sandostatin subcutaneous injection. The effective blood levels of octreotide (as measured by maximal GH inhibition) are well established clinically based on data from decades of octreotide injections.

The study outcomes support advancement of clinical development of Octreolin and allow dose selection for the pivotal study in which the clinical efficacy of Octreolin will be tested in acromegaly patients.

Shlomo Melmed, MD, Senior Vice President, Academic Affairs & Dean of the Medical Faculty at Cedars-Sinai Medical Center and Professor and Associate Dean of the University of California, Los Angeles (UCLA) School of Medicine, said, "Chiasma has demonstrated achievement of an important first clinical step in the process of developing a safe and effective oral therapy for acromegaly patients who would prefer the convenience of oral therapy and the avoidance of the side effects associated with injectable forms of somatostatin analogs."

Portal Hypertension (PHT) --- A New Indication for Octreolin

In addition, Chiasma announced that it is developing Octreolin also as a chronic treatment for patients with PHT; a trial for this new indication (no drugs are approved for portal hypertension in the US) is expected to start in December of 2010.

How Octreolin Works

Octreolin is a product in capsule form that contains octreotide acetate, a 1.0 kDa peptide, and the Company's unique Transient Permeability Enhancer (TPE) technology. The TPE system allows its drug cargo to cross mucosal epithelia in the small intestine by inducing a temporary opening of the Tight Junctions that seal and regulate passage between cells (the paracellular route). This effect on the epithelia is rapid and fully reversible. The drug reaches the bloodstream effectively in its native active form.

TPE activity is the result of a unique combination of excipients assembled in a process leading to a suspension of hydrophilic particles in a lipophilic medium. Chiasma has developed a unique, simple and cost effective production process that ensures safety and stability of its drug products; all components used in manufacturing of the drug product are approved for pharmaceutical use. The TPE technology is versatile, can be applied to a wide range of therapeutic agents and requires no chemical modification of the drug.

About Acromegaly

Acromegaly is an endocrine condition associated with a benign adenoma in the pituitary gland, which secretes excess GH and stimulates excess production of insulin-like growth factor I (IGF-I) by the liver, causing tissue growth throughout the body. The most common signs and symptoms associated with acromegaly include swelling of the hands and feet, enlarged lip, nose, and tongue, joint pain and degenerative arthritis, and an enlarged heart and other organs. Even well controlled patients have an increased risk for mortality; and in poorly controlled patients, cardiovascular, respiratory, endocrine, and metabolic morbidities result in standardized mortality ratios of 2.5 when compared to non-acromegaly populations.¹

Injectable (subcutaneous and intramuscular) somatostatin analogs, which bind to somatostatin receptors (SSTR2, SSTR5) to inhibit GH secretion, are the therapeutic standard of care for acromegaly patients who are not cured by resection of the tumor; surgery is the first line of treatment. GH inhibition by octreotide, one such analog in clinical use, reduces or reverses morbidity and mortality associated with acromegaly. There is a well-defined correlation between plasma levels of octreotide (pharmacokinetics [PK]) and GH reduction (pharmacodynamics [PD]). Clinical endpoints include suppression of GH and normalization of IGF-I levels.²

Treatment normally begins with subcutaneous injections of the short acting (immediate release) octreotide acetate, three times a day. Once a patient's tolerability and responsiveness to the treatment has been proven, Sandostatin LAR (depot formulation), a monthly IM injection, is usually the treatment of choice for life. Octreotide is effective for 95% of the patients; approximately 65% and 30% of patients show a complete or partial response, respectively. However, the injections cause discomfort and pain, with 30% to 50% of patients reporting pain at the injection site (for doses of 20 mg and 30 mg Sandostatin LAR). Patients can also suffer from welts that take a considerable period of time to disappear. In addition, patient needle-phobia can manifest itself in non-compliance as well as stress and anxiety for those who ultimately do take the injections. Furthermore, the octreotide long-acting injections require complex reconstitution and caregivers' assistance, frequently necessitating visits to physician offices.

The pool of patients eligible for Octreolin treatment is estimated to be between 10,000 and 15,000 in the US and an equal number in Europe.

¹ Melmed et al., Guidelines for Acromegaly Management, J Clin Endocrinol Metab, May 2009, 94(5):1509-1517

² Sandostatin, octreotide acetate, Injection, Rx Only, Prescribing Information

About Portal Hypertension (PHT)

PHT has many causes, including liver cirrhosis and portal vein thrombosis, and often leads to the development of esophageal varices that may rupture and bleed, which can be a life-threatening event. There are no approved chronic or oral treatments for PHT in the US; off-label usage of beta (β) blockers is common. However, the effectiveness of β -blockers is not satisfactory for PHT and, in addition, ~30% of patients cannot take β -blockers due to contraindications or significant side effects.

In the acute setting (during a bleeding event), patients may undergo a surgical procedure known as band ligation and receive an IV infusion of octreotide to reduce portal hypertension. In addition to having an effect on GH and IGF-1 levels in patients with acromegaly, somatostatin analogs such as octreotide are known to be potent vasoconstrictors that reduce blood flow and decrease portal pressure.

Since Octreolin is an oral drug, it will be tested to determine if it enables continuation of portal hypertension inhibition once patients are stabilized and discharged from the hospital.

Octreolin is designed to improve patient quality of life, prevent or reduce bleeding events and lower mortality rates of PHT patients, of which there are 80,000 in the US, and an equal number in Europe. Octreolin for PHT will be the subject of Orphan Drug applications in the US and Europe and will be developed under the auspices of the 505(b)(2) regulatory pathway in the US and its EMEA equivalent, the Hybrid Application.

Management Remarks

Roni Mamluk, PhD, Chief Operating Officer said, "This first proof-of-concept of the utility of the TPE technology in humans is promising not only for the Octreolin product and potentially the many patients that will benefit from its use if approved, but also for the validation of the platform for other drugs that we are developing. Our research pipeline includes small molecules, peptides and proteins that could not only benefit from a switch to oral delivery but importantly will be studied in new indications as well as in those instances in which improved labels could significantly augment efficacy or reduce side effects."

Fredric Price, Chairman and CEO commented, "Our corporate strategy is two-fold: (1) to develop our own proprietary products and seek out partnerships outside of the US after demonstrating clinical effectiveness and safety; and (2) to enter into arrangements with companies whose important drugs could benefit from the TPE technology.

"Our internally-developed pipeline is focused on developing new therapies by selecting approved macromolecules that are currently available in injectable form, changing the route of administration to oral and evaluating them for new indications, thereby creating new drugs that will take advantage of the 505(b)(2) regulatory route in the US and similar regulations in other countries.

“Our first collaboration is with Novartis for use of TPE with a product marketed by Novartis and for use with certain other related Novartis products in development.”

About Chiasma

Chiasma applies its proprietary technology to approved drugs, which not only enables their being switched from injectable to oral, but importantly can result in new indications and/or enhanced absorption. The Company’s TPE technology promotes the delivery of drugs to the GI wall and from there to the liver. It is applicable to macromolecules that to-date can be administered only by injection. TPE can be utilized also with small molecules that are already orally available but are poorly absorbed.

The Company has successfully demonstrated proof-of-principle in delivering small proteins, peptides, saccharides and heretofore-insoluble small molecules via the oral route.

Chiasma is backed by ARCH Venture Partners, MPM Capital, F2 Ventures, 7 Health Ventures and the MPM Novartis Strategic Fund.

The Company’s Chairman & CEO is Fredric Price, formerly Chairman of Omrix Biopharmaceuticals and Chairman & CEO of BioMarin Pharmaceutical; he is located in New York. The company’s Chief Operating Officer is Roni Mamluk, PhD, formerly head of preclinical at Adnexus Therapeutics. She led the discovery of the TPE technology and currently is heading operating departments at the Company’s facilities (including laboratories and GMP pilot plant) in Jerusalem.

Chiasma is a Delaware corporation with a 100% owned Israeli subsidiary.

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

Forward-Looking Statements

This press release contains forward-looking statements about the business, goals and prospects of Chiasma, Inc., including, without limitation, statements about the development of drugs in the TPE system. These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. Chiasma is under no obligation, and expressly disclaims any obligation, to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

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