Insmed Provides Update on iPlex Pivotal Trial Data in Severe Primary IGF-1 Deficiency

RICHMOND, Va., Sep 29, 2005 (BUSINESS WIRE) -- Insmed Incorporated (NASDAQ: INSM) provided an update on its ongoing pivotal clinical trial of iPlex(TM) (rhIGF-1/rhIGFBP-3) (Mecasermin rinfibate) for the treatment of children with growth failure who suffer from Severe Primary IGF-1 (insulin-like growth factor-1) deficiency (Primary IGFD). Some of these data were recently featured in a podium presentation at the European Society of Pediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society's 7th Joint Meeting. The data demonstrated that as a once-daily IGF-1 therapy, iPlex safely and significantly increased height velocity, the primary endpoint of the study, in children with short stature due to Severe Primary IGF-1 deficiency.

Cecelia Camacho-Hubner, M.D., of St. Bartholemew's Hospital, London, United Kingdom commented, "Treatment with twice daily injections of rhIGF-I and once-daily injections of rhIGF-I/rhIGFBP-3 complex are effective in promoting linear growth in children with Severe Primary IGF-1 deficiency. Patients with Severe Primary IGF-1 deficiency are susceptible to spontaneous hypoglycemia; therefore it is important to monitor blood glucose levels before initiating any hormonal treatment. It is our opinion that the complex has demonstrated a superior safety profile in children with Severe Primary IGF-1 deficiency, especially regarding the number of hypoglycemic events and the severity of those events. This is most likely due to the modulating effects of IGFBP-3. Once a day injections with rhIGF-I/rhIGFBP-3 has been associated with very good compliance in our patients".

Data Summary:

Efficacy-

-- All patients were pre-pubertal and identified as having Severe Primary IGF-1 deficiency (including subjects with GH receptor deficiency and GH gene deletion). The patients were characterized with severe short stature, low blood levels of IGF-1, and normal to elevated growth hormone levels.

-- All patients received once-daily injections of iPlex at doses of 0.5 - 2.0 mg/kg, with the goal of restoring and maintaining IGF-1 blood levels in the normal range.

-- 25 of the initial 29 patients enrolled in the study were evaluated for the primary efficacy endpoint: change in annualized height velocity (growth rate) after 6 months of treatment. Additional analyses were performed looking at longer-term treatment.

-- The average pre-treatment height velocity in these 25 children was 3.0 centimeters per year (1.2 inches per year). Increases in height velocity during treatment were related to both the iPlex dose received and the IGF-1 blood levels achieved. In a subset of patients (n=16) treated at a low fixed dose (up to 1.0 mg/kg), a better height velocity was observed in those whose IGF-1 blood levels reached a normal target range than in those with persistently low IGF-1 levels on this dose (8.3 vs 5.6 cm/yr at Month 12, respectively). The overall increase in height velocity in this subset of patients was highly statistically significant (p

-- The importance of adjusting dose to optimize IGF-1 blood levels was demonstrated in the second subset of patients (n=9), whose dose was increased up to 2.0 mg/kg based on IGF-1 levels and clinical outcome. The average 9-month annualized height velocity in this group was 8.2 cm/yr, a 6.0 cm/yr increase over their average pre-treatment height velocity of 2.2 cm/yr (p

-- Since iPlex therapy includes the important binding protein IGFBP-3, which is administered with the IGF-1 in a stable complex of the 2 recombinant proteins, the baseline IGFBP-3 levels were not a consideration when dosing the patients.

Safety

-- Once daily administration of up to 2.0 mg/kg of iPlex was found to safe and well tolerated.

-- Low blood sugar (hypoglycemia) can occur due to the insulin-like effects of IGF-1. However, the frequency of severe hypoglycemia in this iPlex study appeared to be less frequent than that reported in published studies of free rhIGF-1 therapies. No hypoglycemic convulsions or cases of facial nerve paralysis occurred in the iPlex study, both of which are serious adverse events that have been associated with free IGF-1 therapies in published studies.

-- As with all protein products, a proportion of patients developed antibodies to the product. After extensive testing, there was no evidence that the antibodies resulted in neutralization of biologic activity, such as reduced height velocity, nor adverse drug reactions or physical findings.

-- A matched safety comparison was performed of this study with a similar, prospectively-designed, published clinical study of free rhIGF-1 (manufactured by Pharmacia Inc.) in children with Severe Primary IGF-1 deficiency . A two-fold higher incidence of serious adverse events (SAE's) occurred in the free IGF-1 study as compared with the SomatoKine study over a similar time frame.

About Severe Primary IGF-1 deficiency

Severe Primary IGF-1 deficiency encompasses a variety of genetic and acquired conditions in which the action of growth hormone (GH) is absent or severely attenuated, resulting in low serum levels of IGF-1. Because IGF-1 is the primary mediator of the growth-promoting actions of GH, SomatoKine replacement therapy in children with Severe Primary IGF-1 deficiency is intended to bypass the blocked actions of GH by replacing the deficient IGF-1, resulting in improved growth.

More on iPlex

Insmed's iPlex is a proprietary drug product for the delivery of recombinant insulin-like growth factor I (IGF-1). It is administered as a preformed complex with a recombinant form of its natural binding protein, insulin-like growth factor binding protein 3 (rhIGFBP-3). The novel compound is administered as a once-daily subcutaneous injection, which can restore and maintain IGF-1 levels to physiologically relevant levels. The binding protein (rhIGFBP-3) extends the residence time of IGF-1 in the blood, conferring a superior pharmacokinetic profile as compared with rhIGF-1 alone. In the bound state, the IGF-1 is inactive, and remains so until delivered to target tissues in the body where it is released and becomes biologically active. This reduces the risk of short- and long-term safety concerns that have been associated with unrestrained levels of free IGF-1.

iPlex has been investigated in a number of other indications in addition to growth disorders. In patients with Type 1 and Type 2 diabetes, administration of iPlex demonstrated a significant improvement in blood sugar control and a significant reduction in daily insulin use. In children and adults suffering severe burn injury, administration of iPlex demonstrated a significant improvement in muscle protein synthesis and a significant reduction in the inflammatory response associated with the trauma. In elderly individuals recovering from hip fractures, administration of iPlex demonstrated a significant improvement in functional recovery and bone mineral density. In addition to the Severe Primary IGF-1 deficiency program, iPlex is currently being studied in a Phase II clinical trial at the University of California, San Francisco in patients with HIV-Associated Lipodystrophy, and in a Phase II clinical trial at the University of Cambridge, U.K., in patients with Extreme Insulin Resistance.

About Insmed

Insmed is a biopharmaceutical company focused on the discovery and development of drug candidates for the treatment of metabolic diseases and endocrine disorders. For more information, please visit www.insmed.com.

Statements included within this press release, which are not historical in nature, may constitute forward-looking statements for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Forward-looking statements in this press release include, but are not limited to, statements regarding clinical trials and goals, our regulatory and business strategies and growth opportunities for existing or proposed products. Such forward-looking statements are subject to numerous risks and uncertainties, including risks that product candidates may fail in the clinic or may not be successfully marketed or manufactured, the company may lack financial resources to complete development of product candidates, the FDA may interpret the results of our studies differently than we have, competing products may be more successful, demand for new pharmaceutical products may decrease, the biopharmaceutical industry may experience negative market trends and other risks detailed from time to time in the company's filings with the Securities and Exchange Commission. As a result of these and other risks and uncertainties, actual results may differ materially from those described in this press release. For further information with respect to factors that could cause actual results to differ from expectations, reference is made to reports filed by the Company with the Securities and

Exchange Commission under the Securities Exchange Act of 1934, as amended. The forward-looking statements made in this release are made only as of the date hereof and Insmed disclaims any intention or responsibility for updating predictions or financial guidance contained in this release.