



**IRONSHORE**

PHARMACEUTICALS & DEVELOPMENT, INC.

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For Immediate Release:

## **IRONSHORE PHARMACEUTICALS PRESENTS NEW PIVOTAL TRIAL DATA AT AACAP MEETING**

George Town, Grand Cayman, October 28, 2016—Ironshore Pharmaceuticals & Development, Inc. (“Ironshore”), a wholly owned subsidiary of Highland Therapeutics Inc., today announced the presentation of previously embargoed data at the American Academy of Child and Adolescent Psychiatry annual conference in New York, NY. The data are from a Pivotal Phase-3 clinical trial of HLD200, a delayed-release and extended-release formulation of methylphenidate currently in development. The novel medication, which is dosed at night, is being developed with the objective of reducing functional impairments and symptoms associated with Attention-Deficit/Hyperactivity Disorder (ADHD), immediately upon awakening, throughout the day and into the evening/bedtime period. In addition to a comprehensive period of coverage, HLD200 is also being developed with the objective of providing improved consistency of clinical effect throughout the day. These attributes, which may represent a potential paradigm shift in the management of ADHD, can be attributed to DELEXIS®, Ironshore’s innovative drug delivery technology that could have meaningful impact on human health outcomes in a variety of therapeutic areas including central nervous system disorders and inflammatory bowel disease.

The newly released data from the pivotal trial (HLD200-108) demonstrate a robust clinical effect in HLD200-treated patients, compared with placebo, based on the Before School Functioning Questionnaire (BSFQ) and the Parent Rating of Evening and Morning Behavior – Revised (PREMB-R) AM subscale. Both validated rating scales, which measure functional impairments during the early morning period in a pediatric population, were key secondary endpoints in the trial.

One hundred and sixty-one (161) ADHD patients, ages 6-12, were enrolled into the study. Average BSFQ baseline scores were 44.2 and 44.9 in the HLD200 (n=81) and placebo (n=80) groups, respectively. After a three-week, forced/flexible dose-titration period, average BSFQ scores decreased 58% and 36%, respectively, demonstrating a statistically significant improvement in favor of the HLD200-treated patients, ( $p < 0.001$ ).

This improvement was also reflected in PREMB-R AM scores. At baseline, patients in the drug and placebo arms of the study had PREMB-R AM scores of 6.4 and 5.8, respectively. Following the treatment period, those scores decreased 61% and 40%, respectively, demonstrating a statistically significant improvement in favor of the HLD200-treated patients, ( $p = 0.002$ ). This treatment effect was replicated in the HLD200-107 study, where HLD200 showed a statistically significant improvement, compared with placebo, based on the PREMB-R AM scale ( $p < 0.001$ ).

“This is a time for renewed optimism for patients with ADHD and the physicians that treat them,” said David Lickrish, Ironshore’s Chief Executive Officer. “I believe that, for the first time since the introduction of once-daily ADHD medications in 2000, science has advanced to the degree where clinically meaningful improvements in patient outcomes may be achieved with advanced drug-delivery technologies.”

Of note, the HLD200-108 data demonstrated the persistence of the clinically meaningful treatment effect into the evening bedtime period as measured by the PREMB-R PM subscale, which was also a key secondary endpoint in the trial. At baseline, average PREMB-R PM scores were 17.4 and 16.6 for the HLD200 and placebo groups, respectively. At the end of the treatment period, HLD200-treated patients showed a 43% decrease in their PREMB-R PM scores, compared with 25% for the placebo group, a statistically significant improvement favoring HLD200 ( $p < 0.001$ ). This treatment effect was replicated in the HLD200-107 study, where HLD200 showed a statistically significant improvement, compared with placebo, based on the PREMB-R PM scale ( $p = 0.003$ ).

Commenting on the results, Dr. Randy Sallee, Chief Medical Officer said, “The clinically meaningful and statistically significant improvements seen with HLD200 across multiple distinct rating scales that measure functional impairments during the morning period, suggest that physicians may, for the first time, soon have a treatment option for millions of struggling families. The PREMB-R PM scores, replicated across two pivotal studies, show the persistence of clinical effect through the evening period. If approved by the FDA, I believe HLD200 will be a game-changer for the treatment of ADHD, given its comprehensive treatment effect throughout the entire day. To our knowledge, HLD200-108 is the first study to demonstrate significant

improvements in each of early morning, late afternoon and evening impaired functioning with a single dose of a long-acting stimulant in children with ADHD.”

In terms of safety, HLD200 was generally well tolerated with no serious treatment-emergent adverse events (TEAEs) reported. The vast majority of TEAEs were mild to moderate in severity and resolved during the course of the study. Across all clinical studies conducted with HLD200, the product’s adverse event profile is consistent with other stimulants on the market and with the known effects of methylphenidate.

“Based on my experience as a clinical investigator with HLD200, this medicine has the potential to live up to the promise of a paradigm shift in the management of ADHD,” said Dr. Andrew J. Cutler, a Board-Certified Psychiatrist and Chief Medical Officer of Meridien Research in Bradenton, FL.

#### **About Ironshore Pharmaceuticals & Development, Inc.**

Ironshore Pharmaceuticals & Development, Inc., a wholly owned subsidiary of Highland Therapeutics Inc., is a specialty pharmaceutical company that is leveraging its proprietary technology, DELEXIS®, to optimize the delivery of previously approved drug products. Highland Therapeutics Inc. is a client of MaRS Discovery District’s Health Venture Services group, which provides advisory services, connections to talent, customer & capital networks, and market intelligence to high-impact, Ontario-based life sciences ventures, helping them commercialize their ideas and build globally competitive companies.

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#### **Forward-Looking Statements**

This press release contains forward-looking information, which reflects Ironshore’s current expectations regarding future events. Forward-looking information is based on a number of assumptions and is subject to a number of risks and uncertainties, many of which are beyond Ironshore’s control that could cause actual results and events to differ materially from those that are disclosed in or implied by such forward-looking information. These forward-looking statements are made as of the date of this press release and, except as expressly required by applicable law, Ironshore assumes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.