Millendo Therapeutics Announces Positive Topline Phase 2 Results of ATR-101 in Classic Congenital Adrenal Hyperplasia

-- FDA grants orphan drug designation based on trial results --

ANN ARBOR, Mich., November 8, 2017 – Millendo Therapeutics, Inc., a clinical-stage biopharmaceutical company focused on developing novel treatments for endocrine diseases, today announced positive topline results from a Phase 2 proof-of-concept study of ATR-101 in classic congenital adrenal hyperplasia (CAH), a rare inherited endocrine disease characterized by abnormal hormone levels and overgrowth of the adrenal glands.

In the Phase 2 study, 7 of the first 10 patients demonstrated a clear biological effect as measured by reductions in 17-hydroxyprogesterone (17-OHP), a key measure of disease control. Based on the trial results, Millendo ended the trial early and the U.S. Food and Drug Administration (FDA) has granted orphan drug status to ATR-101 in this indication.

“The encouraging topline results announced today support the further clinical development of ATR-101 in classic congenital adrenal hyperplasia, a disease for which current treatment options are limited and are associated with significant side effects,” said Julia Owens, Ph.D., President and Chief Executive Officer, Millendo Therapeutics. “In this clinical trial, ATR-101 added to existing treatment with glucocorticoids was well-tolerated and demonstrated promising reductions in 17-OHP. ATR-101 also exhibited rapid onset of action with reductions in key steroids and steroid precursors. Significant reductions in steroidogenesis were seen even in patients with unusually high 17-OHP levels at baseline.”

Enrollment in the trial was stopped at 10 patients due to the demonstration of a clear biological effect in 7 patients with marked reductions in 17-OHP. Mean reductions in 17-OHP were observed at all ATR-101 doses while mean increases were observed during all placebo treatments. Two patients experienced a reduction in 17-OHP levels to ≤2x ULN, the primary endpoint, a result consistent with the short duration of treatment (2 weeks/dose level) and high baseline levels. ATR-101 was well-tolerated at all dose levels. Millendo will present full results at an upcoming medical meeting.

“Treatment of patients with classic congenital adrenal hyperplasia is a difficult balance between the morbidities of androgen excess resulting from undertreatment with glucocorticoids and the morbidities of excess glucocorticoids due to overtreatment,” said Richard Auchus, M.D., Ph.D., Professor of Internal Medicine and Professor of Pharmacology, University of Michigan. “While additional studies will need to be carried

out, the results of this Phase 2 trial of ATR-101 give promise to patients in need of improvement with hormonal imbalances seen in CAH."

The U.S. FDA granted orphan drug status to ATR-101 based on the demonstrated activity of the drug in this trial as well as the size of the patient population living with CAH. The prevalence of CAH is estimated at approximately 1 in 10,000 to 1 in 15,000 births in North American and European populations[1].

Separately, Millendo has decided to discontinue development of MLE4901 after assessment of the clinical risks and benefits of the program.

About the Phase 2 Trial
The Phase 2 clinical trial was a multi-center, single-blind, multiple dose proof-of-concept study that assessed the efficacy and safety of orally-administered ATR-101 in addition to corticosteroids in patients with classic congenital adrenal hyperplasia resulting from 21-hydroxylase deficiency. The study, which assessed 5 escalating doses, alternated between 2 weeks of treatment with ATR-101 and 2 weeks with placebo to determine the effects of ATR-101 on adrenal steroids. For additional information on this clinical trial, please visit www.clinicaltrials.gov and reference ID#: NCT02804178.

About ATR-101
ATR-101 is a selective inhibitor of ACAT1 (acyl-CoA:cholesterol acyltransferase 1), an enzyme that catalyzes the transformation of free cholesterol into cholesterol ester, the starting point for adrenal steroid synthesis. In preclinical studies, ATR-101 was observed to be associated with dose and time-dependent decreases in levels of all adrenal steroids and steroid precursors, including those particularly elevated in CAH. ATR-101 is also in Phase 2 development for Cushing's syndrome (NCT03053271) and Phase 1 development for adrenocortical carcinoma (NCT01898715) at clinical sites in the U.S. and Europe.

About Classic Congenital Adrenal Hyperplasia
Classic congenital adrenal hyperplasia (CAH) is a rare inherited endocrine disease caused by a genetic mutation in a crucial enzyme for cortisol synthesis and is characterized by overgrowth of the adrenal glands, adrenal insufficiency, mineralocorticoid deficiency, and androgen excess. The most frequent cause of CAH, responsible for 95% of cases, is a deficiency in the enzyme 21-hydroxylase, which is required for the production of cortisol and aldosterone in the adrenal glands. Classic CAH is diagnosed at birth and is characterized by adrenal insufficiency. It can lead to severe virilization in women, testicular tumors in men, and infertility.

About Millendo Therapeutics
Millendo Therapeutics is focused on developing novel treatments for endocrine diseases. Our mission is to build a leading endocrine company that creates distinct and transformative treatments for a wide range of diseases where there is a significant unmet medical need. We are currently advancing ATR-101 for the treatment of three

different orphan adrenal diseases; classic congenital adrenal hyperplasia, endogenous Cushing's syndrome, and adrenocortical carcinoma. www.millendo.com

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[1] Speiser PW, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2010 Sep;95(9):4133-60. (PMID: 20823466)