Achievement of Primary Endpoint in Phase 3 Study of Pegzilarginase in Patients with Arginase 1 Deficiency

Immedica Pharma AB is pleased to announce the successful outcome from the **Pegzilarginase Phase 3 Study**, presented earlier today by our valued partner Aeglea BioTherapeutics, Inc. (see full press release below). Anders Edvell, CEO says: "I am pleased to see that these study results give hope for improved treatment options for patients with the severe and debilitating disease arginase-1 deficiency. Immedica plans to submit an EMA-application in 2022 which, if approved, will mark an important milestone in Immedica's ambition to bring new innovative medicines for the patient group within Urea Cycle Disorders."

The pressrelease from Aeglea BioTherapeutics, Inc. follows below.

Aeglea BioTherapeutics Announces Achievement of Primary Endpoint in Phase 3 Study of Pegzilarginase in Patients with Arginase 1 Deficiency

80% plasma arginine reduction (primary endpoint; $p < 0.0001$) accompanied by a positive trend in GMFM-E, a key clinical assessment of patient mobility

90.5% of patients achieved normal plasma arginine levels

Pegzilarginase was well-tolerated; no discontinuations due to adverse events

First potential therapy to address key driver of ARG1-D, a devastating ultra-rare disease

Plan to submit BLA in first half of 2022

Company to host conference call and webcast today at 8:00am EST

AUSTIN, Texas, December 6, 2021 — Aeglea BioTherapeutics, Inc. (NASDAQ: AGLE), a clinical-stage biotechnology company developing a new generation of human enzyme therapeutics as innovative solutions for rare metabolic diseases, today announced that the pivotal Phase 3 study, PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints), met the primary endpoint with a statistically significant reduction in plasma arginine from baseline after 24 weeks of treatment with pegzilarginase ($p < 0.0001$). Importantly, pronounced and sustained plasma arginine reduction was accompanied by a positive trend in Gross Motor Function Measure Part E (GMFM-E), a key clinical assessment of a patient's mobility, including the ability to walk, run and jump.

PEACE is the first placebo-controlled clinical trial ever conducted in Arginase 1 Deficiency (ARG1-D) and pegzilarginase is the first potential therapy to normalize the markedly elevated plasma arginine levels in these patients. Based on the results of this trial, Aeglea plans to submit a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) in the first half of 2022. Additionally, Aeglea will work with Immedica Pharma AB, its commercial partner in Europe and certain countries in the Middle East, to submit marketing authorization applications in those territories.

“I have been treating children born with ARG1-D for 20 years and what we are experiencing with pegzilarginase has truly given us a renewed sense of optimism. These children and their families live with a daily burden of not only managing the progressive manifestations of the disease, including mobility limitations, intellectual disability and behavior challenges, but also a burdensome standard of care. A better treatment paradigm for these patients is desperately needed,” said Dr. George Diaz, Director, Program for Inherited Metabolic Disorders at Mount Sinai Hospital, New York, NY and PEACE trial principal investigator.

“Clinicians recognize the importance of effective arginine control, and I am delighted that the PEACE pivotal trial demonstrated that pegzilarginase lowered plasma arginine to normal levels and also showed a positive trend in an important mobility assessment of clinical benefit. I believe that, with early diagnosis and treatment intervention, families have a new reason to hope.”

ARG1-D is a rare, progressive and debilitating disease characterized by high levels of the amino acid arginine. The disease manifestations include spasticity, developmental delay, intellectual disability and seizures. The functional disability and impact on daily life creates a significant burden for patients and caregivers. There are currently no FDA-approved treatments that address elevated arginine, the key driver of ARG1-D. Current standard of care includes severe dietary protein restriction and essential amino acid supplementation, which does not effectively or sustainably reduce high arginine levels.

PEACE is a global, randomized, double-blind, placebo-controlled trial that enrolled 32 patients with ARG1-D aged two years and older. The study was designed to assess the effects of treatment with pegzilarginase (n=21) versus placebo (n=11) from baseline through a prespecified 24-week treatment period. The primary endpoint assessed plasma arginine reduction from baseline levels. The key secondary endpoint evaluated mobility using GMFM-E, which consists of 24 tasks involving walking forward/backward, running, jumping and ascending/descending stairs, and the 2-Minute Walk Test (2MWT), a measure of the distance a patient walks in two minutes. Other secondary endpoints included additional outcome assessments, safety and pharmacokinetics. Topline results are summarized as follows:

- PEACE demonstrated a highly statistically significant 80% reduction in mean plasma arginine in pegzilarginase treated patients ($p<0.0001$), the primary endpoint of the trial. Importantly, normal plasma arginine levels (40-115µM) were achieved in 90.5% of pegzilarginase treated patients compared to none of the patients in the placebo arm.
- The least squares mean GMFM-E score improved by 4.2 units for pegzilarginase treated patients and worsened by 0.4 units in the placebo arm ($p=0.1087$; 95% CI [-1.1, 10.2]), establishing a positive trend in this mobility assessment. The least squares mean 2MWT distance increased 7.4 meters in pegzilarginase treated patients and 1.9 meters in the placebo arm ($p=0.5961$; 95% CI [-15.6, 26.7]).
- Pegzilarginase was well-tolerated and safety data were consistent with results from previous clinical trials. There were no study discontinuations due to adverse events.

All 31 patients who completed the 24-week double-blind study period continued into the Long-Term Extension (LTE) portion of the PEACE trial. In addition, 13 of the 14 patients in the ongoing Phase 1/2 Open Label Extension (OLE) trial have continued pegzilarginase therapy ranging from 2 to 4 years. The previously presented 56-week data from the Phase 1/2 OLE trial supports the long-term clinical benefit of pegzilarginase treatment. The company believes that the entirety of data from the pegzilarginase program supports the long-term clinical benefit of pegzilarginase in ARG1-D. Additional data from the pegzilarginase program are expected to be presented at upcoming medical meetings and submitted to peer-reviewed medical journals.

“I would like to thank the patients and their caregivers, investigators and staff, and our employees for their contributions to the study. The dramatic reduction in plasma arginine levels and the positive trend in GMFM-E are very encouraging and represent an important step in our

mission to bring a transformative therapy to this underserved patient community," said Anthony G. Quinn, M.B., Ch.B., Ph.D., president and chief executive officer of Aeglea. "We believe that today's announcement demonstrates validation of our scientific platform, overall pipeline and potential to address other rare metabolic diseases."

To access archived Investor Conference webcasts, visit the Events & Presentations section of the Company's website. A replay of Company webcasts is archived on the website for 60 days following presentations.

About the Phase 3 PEACE Study

PEACE is a single, global, randomized, double-blind, placebo-controlled trial that enrolled 32 patients aged 2 years and older with Arginase 1 Deficiency in the United States, Canada and Europe (NCT03921541). PEACE was designed to assess the effects of treatment with pegzilarginase versus placebo over 24 weeks with a primary endpoint of plasma arginine reduction from baseline. Secondary endpoints include clinical outcome assessments focused on several mobility assessments, in addition to safety and pharmacokinetics. Patients were randomized on a two-to-one basis to receive weekly infusions of pegzilarginase or placebo for the double-blind 24-week treatment period.

About Pegzilarginase in Arginase 1 Deficiency

Pegzilarginase is a novel recombinant human enzyme engineered to degrade the amino acid arginine and which has been shown to rapidly and sustainably lower levels of the amino acid arginine in plasma. Aeglea is developing pegzilarginase for the treatment of people with Arginase 1 Deficiency (ARG1-D), a rare debilitating and progressive disease characterized by the accumulation of arginine. ARG1-D presents in early childhood and patients experience spasticity, seizures, developmental delay, intellectual disability and early mortality.

Aeglea's Phase 1/2 and Phase 2 Open Label Extension (OLE) data for pegzilarginase in people with ARG1-D demonstrated clinical improvements and sustained lowering of plasma arginine. Pegzilarginase has received multiple regulatory designations, including Rare Pediatric Disease, Breakthrough Therapy, Fast Track and Orphan Drug Designations from the U.S. Food and Drug Administration as well as Orphan Drug Designation from the European Medicines Agency.

About Aeglea BioTherapeutics

Aeglea BioTherapeutics is a clinical-stage biotechnology company redefining the potential of human enzyme therapeutics to benefit people with rare metabolic diseases with limited treatment options. Aeglea's lead product candidate, pegzilarginase, is in an ongoing Phase 3 pivotal trial in patients with Arginase 1 Deficiency and has received both Rare Pediatric Disease and Breakthrough Therapy designations. Aeglea has an ongoing Phase 1/2 clinical trial of AGLE-177 for the treatment of Homocystinuria. AGLE-177 has been granted Rare Pediatric Disease Designation. Aeglea has an active discovery platform focused on engineering small changes in human enzymes to have a big impact on the lives of patients and their families.

Safe Harbor / Forward Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from what we expect. Examples of forward-looking statements include, among others, statements we make regarding our ability to obtain regulatory approval for, and commercialize, pegzilarginase, recognize milestone and royalty payments from our agreement with Immedica, the timing and success of our clinical

trials and related data, the timing and expectations for regulatory submissions and approvals, including the submission of a BLA for pegzilarginase, timing and results of meetings with regulators, the timing of announcements and updates relating to our clinical trials and related data, our ability to enroll patients into our clinical trials, the expected impact of the COVID-19 pandemic on our operations and clinical trials, success in our collaborations, our cash forecasts, the potential addressable markets of our product candidates and the potential therapeutic benefits and economic value of our lead product candidate or other product candidates. Further information on potential risk factors that could affect our business and financial results are detailed in our Annual Report on Form 10-K for the year ended December 31, 2020 and our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 filed with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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