



Rocket Pharmaceuticals Reaches FDA Alignment on Pivotal Phase 2 Trial Design for RP-A501 in Danon Disease

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Final alignment reached on a 12 patient, single-arm, open label study with a biomarker based co-primary endpoint assessed at 12 months to support accelerated approval

Co-primary endpoint consisting of LAMP2 protein expression and Left Ventricular (LV) Mass change from baseline

CRANBURY, N.J.--(BUSINESS WIRE)--Sep. 12, 2023-- [Rocket Pharmaceuticals, Inc.](#) (NASDAQ: RCKT), a leading late-stage biotechnology company advancing an integrated and sustainable pipeline of genetic therapies for rare disorders with high unmet need, today announced that alignment has been reached with the Food and Drug Administration (FDA) on the global Phase 2 pivotal trial of RP-A501 for Danon Disease. Danon Disease is a uniformly fatal inherited cardiomyopathy that leads to mortality in the majority of male patients at age ~20 and females at age ~40, and for which there are no approved curative or disease-modifying therapies. The disease affects an estimated 15,000 to 30,000 patients in the U.S. and Europe.

"I am very excited to announce our alignment with the FDA on our pivotal study design for RP-A501 for Danon Disease, which reflects the highly collaborative discussions with the review team and senior management at FDA's Center for Biologics Evaluation and Research and marks the first-ever regulatory pathway to approval for a genetic treatment for heart disease. We believe this milestone sets us on the most efficient and rapid path to delivering this potentially transformative therapy to Danon Disease patients who would otherwise progress to heart transplantation or death," said Gaurav Shah, M.D., Chief Executive Officer, Rocket Pharma. "I would also like to highlight the work conducted by our CMC team over the past several years to establish our in-house cGMP manufacturing capabilities, which has already provided us with sufficient material for the pivotal study and should support our eventual commercialization efforts."

Dr. Shah continued "As a one-time potentially curative infusion, RP-A501 has the potential to restore normal cardiac function and provide a lifetime of benefit to patients with Danon Disease who have no other viable treatment options. With today's progress in our Danon Disease program, we believe we are forging a path to bring curative gene therapies to patients affected by devastating cardiovascular diseases and broadening the possibilities for addressing the large array of inherited heart diseases through the promise of cardiac gene therapy."

Phase 2 Pivotal Trial of RP-A501 for Danon Disease

The global, single-arm, multi-center Phase 2 pivotal trial will evaluate the efficacy and safety of RP-A501 in 12 patients with Danon Disease, including a pediatric safety run-in (n=2), with a natural history comparator and a dose level of 6.7×10^{13} GC/kg.

- To support accelerated approval, the study will assess the efficacy of RP-A501 as measured by the biomarker-based co-primary endpoint consisting of improvements in LAMP2 protein expression (\geq Grade 1, as measured by immunohistochemistry), and reductions in left ventricular (LV) mass.
- Key secondary endpoint is change in troponin. Additional secondary endpoints will include natriuretic peptides, Kansas City Cardiomyopathy Questionnaire (KCCQ), New York Heart Association (NYHA) class, event free survival to 24 months and treatment emergent safety events. These endpoints could support full approval with longer-term follow-up.
- A global natural history study will serve as an external comparator and run concurrently to the Phase 2 pivotal trial.
- In-house manufacturing has been completed with sufficient high-quality drug product produced to fully supply the Phase 2 pivotal study. Potency assays have been developed and qualified in accordance with FDA guidance.

Filing of the Clinical Trial Application (CTA)/Investigational Medicinal Product Dossier (IMPD) for RP-A501 to enable initiation of EU study activities is anticipated in the third quarter of this year. Additionally, Rocket has secured an ICD-10 code from CMS for LAMP2 deficiency in Danon Disease.

About RP-A501

RP-A501 is Rocket's investigational gene therapy product for the treatment of Danon Disease and the first gene therapy for a cardiovascular condition to demonstrate safety and efficacy in clinical studies. Danon Disease is caused by mutations in the LAMP2 gene. RP-A501 consists of a recombinant adeno-associated serotype 9 (AAV9) capsid containing a full-length, wild-type version of the human LAMP2B transgene (AAV9.LAMP2B) which, when inserted into heart cells harboring mutations in the endogenous LAMP2 gene, has the potential to fully restore cardiac function at its root. RP-A501

represents a single dose treatment and is administered as an intravenous (IV) infusion. In preclinical and clinical studies, AAV9.LAMP2B has been shown to target cardiac cells (cardiomyocytes) and deliver the functional LAMP2B gene to heart tissue, which ultimately leads to improved cardiac structure and function in patients.

About Danon Disease

Danon Disease is a rare X-linked inherited disorder caused by mutations in the gene encoding lysosome-associated membrane protein 2 (LAMP-2), an important mediator of autophagy. This results in accumulation of autophagosomes and glycogen, particularly in cardiac muscle and other tissues, which ultimately leads to heart failure, and for male patients, frequent death during adolescence or early adulthood. It is estimated to have a prevalence of 15,000 to 30,000 patients in the U.S. and Europe. The only available treatment option for Danon Disease is cardiac transplantation, which is associated with substantial complications and is not considered curative. There is a high unmet medical need for patients with Danon Disease.

About Rocket Pharmaceuticals, Inc.

Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT) is advancing an integrated and sustainable pipeline of investigational genetic therapies designed to correct the root cause of complex and rare childhood disorders. The Company's platform-agnostic approach enables it to design the best therapy for each indication, creating potentially transformative options for patients afflicted with rare genetic diseases. Rocket's clinical programs using lentiviral vector (LVV)-based gene therapy are for the treatment of Fanconi Anemia (FA), a difficult to treat genetic disease that leads to bone marrow failure and potentially cancer, Leukocyte Adhesion Deficiency-I (LAD-I), a severe pediatric genetic disorder that causes recurrent and life-threatening infections which are frequently fatal, and Pyruvate Kinase Deficiency (PKD), a rare, monogenic red blood cell disorder resulting in increased red cell destruction and mild to life-threatening anemia. Rocket's first clinical program using adeno-associated virus (AAV)-based gene therapy is for Danon Disease, a devastating, pediatric heart failure condition. Rocket also has received IND clearance for the AAV-based gene therapy program for PKP2-arrhythmic cardiomyopathy (ACM) and is advancing a preclinical program for BAG3-associated dilated cardiomyopathy (DCM). For more information about Rocket, please visit www.rocketpharma.com.

Rocket Cautionary Statement Regarding Forward-Looking Statements

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding the safety and effectiveness of product candidates that Rocket is developing to treat Danon Disease (DD), the expected timing and data readouts of Rocket's ongoing and planned clinical trials, the expected timing and outcome of Rocket's regulatory interactions and planned submissions, Rocket's plans for the advancement of its Danon Disease program, including its planned pivotal trial, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials, may constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995 and other federal securities laws and are subject to substantial risks, uncertainties and assumptions. You should not place reliance on these forward-looking statements, which often include words such as "believe," "expect," "anticipate," "intend," "plan," "will give," "estimate," "seek," "will," "may," "suggest" or similar terms, variations of such terms or the negative of those terms. Although Rocket believes that the expectations reflected in the forward-looking statements are reasonable, Rocket cannot guarantee such outcomes. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Rocket's ability to monitor the impact of COVID-19 on its business operations and take steps to ensure the safety of patients, families and employees, the interest from patients and families for participation in each of Rocket's ongoing trials, patient enrollment, trial timelines and data readouts, our expectations regarding our drug supply for our ongoing and anticipated trials, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials of its product candidates, our ability to submit regulatory filings with the U.S. Food and Drug Administration (FDA) and to obtain and maintain FDA or other regulatory authority approval of our product candidates, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, our competitors' activities, including decisions as to the timing of competing product launches, pricing and discounting, our integration of an acquired business, which involves a number of risks, including the possibility that the integration process could result in the loss of key employees, the disruption of our ongoing business, or inconsistencies in standards, controls, procedures, or policies, our ability to successfully develop and commercialize any technology that we may in-license or products we may acquire and any unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket's Annual Report on Form 10-K for the year ended December 31, 2022, filed February 28, 2023 with the SEC and subsequent filings with the SEC including our Quarterly Reports on Form 10-Q. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and Rocket undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.



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