Rocket Pharmaceuticals Announces FDA Has Lifted the Clinical Hold on the Pivotal Phase 2 Trial of RP-A501 for the Treatment of Danon Disease

August 20, 2025

CRANBURY, N.J.--(BUSINESS WIRE)--Aug. 20, 2025-- Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT), a fully integrated, late-stage biotechnology company advancing a sustainable pipeline of genetic therapies for rare disorders with high unmet need, today announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold on the Company's pivotal Phase 2 trial of RP-A501 for the treatment of Danon disease. The hold was lifted in under three months, underscoring the efficiency of the FDA's review process and Rocket's commitment to expeditiously optimize safety and resume the trial.

In its correspondence, the FDA confirmed that Rocket satisfactorily addressed issues outlined in the clinical hold. The FDA authorized the pivotal study to resume first with a recalibrated dose of 3.8 x 10^{13} GC/kg of RP-A501 in three patients, treated sequentially with a minimum four-week interval between each treatment. This adjusted dose aligns with the lower range of administered doses that were associated with efficacy across multiple biomarkers, echocardiographic and clinical endpoints in the Phase 1 study, and has been determined as most likely to confer the safety and efficacy identified in the low-dose Phase 1 cohorts. In addition, Rocket will collaborate with investigators to implement an immunomodulatory regimen more closely reflecting that administered in the Phase 1 pediatric cohort. The revised regimen discontinues prophylactic use of a C3 complement inhibitor, while maintaining sirolimus, rituximab, and steroids. Additionally, the protocol will specify a lower threshold for administering a C5 inhibitor (eculizumab) in response to impending complement activation.

To date, six patients with Danon disease have been treated in the Phase 2 study with RP-A501. Further updates about the Phase 2 study can be expected following review of data from the next three patients.

RP-A501 Phase 2 Pivotal Trial Overview
The global, single-arm, multi-center 12-patient Phase 2 pivotal trial evaluates the efficacy and safety of RP-A501 for the treatment of Danon disease. The trial began with a pediatric safety run-in (n=2) and treated a total of six patients at a dose level of 6.7 x 10^{13} GC/kg. Per alignment with the FDA upon lifting of the clinical hold, three additional patients are expected to be treated at a dose level of 3.8 x 10^{13} GC/kg with a minimum four-week interval between dosing, followed by additional patients to complete the trial.

- To support accelerated approval, the study assesses the efficacy of RP-A501 as measured by the biomarker-based co-primary endpoint consisting of improvements in LAMP2 protein expression, and reductions in left ventricular mass.
- The key secondary endpoint is change in troponin. Additional secondary endpoints include natriuretic peptides, Kansas City Cardiomyopathy Questionnaire, New York Heart Association 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 is running concurrently with the Phase 2 pivotal trial.
- All patients enrolled in the trial are required to have a three-months observational pre-treatment run-in to enable an assessment of troponin (and other biomarker) trajectories to optimally assess this key secondary endpoint.

Details about the Phase 2 study can be found at www.clinicaltrials.gov under NCT identifier NCT06092034.

About RP-A501
RP-A501 is Rocket's investigational gene therapy for the treatment of Danon disease and the first gene therapy for a cardiovascular condition to demonstrate safety and efficacy in clinical studies. RP-A501 has the potential to restore or stabilize cardiac function in patients with Danon disease.

RP-A501 consists of a recombinant adeno-associated serotype 9 (AAV9) capsid containing a functional version of the human *LAMP2B* transgene (AAV9.LAMP2B) which is administered as a single intravenous (IV) infusion. In clinical studies, RP-A501 has been shown to target cardiac cells (cardiomyocytes) and deliver the functional *LAMP2B* gene to heart tissue, which led to improved cardiac structure and function in patients. RP-A501 holds FDA RMAT, Fast Track, Rare Pediatric, and Orphan Drug designations in the U.S. along with ATMP and PRIME designations in the EU.

About Danon Disease
Danon disease is a rare X-linked inherited, multi-organ lysosomal-associated disorder with a devastating clinical course. The causative mutation has

been identified in the gene encoding for lysosome-associated membrane protein, otherwise known as *LAMP2*, an important mediator of autophagy and primarily expressed in heart, skeletal muscle and brain tissue. This mutation 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. The only available treatment option for Danon disease is cardiac transplantation, which is associated with substantial complications and is not considered curative, representing the high unmet medical need for patients with Danon disease. It is estimated to have a prevalence of 15,000 to 30,000 patients in the U.S. and Europe.

In 2023, Rocket secured an ICD-10 code from the Centers for Medicare and Medicaid Services (CMS) to document patients with LAMP2 deficiency in Danon disease.

About Rocket Pharmaceuticals, Inc.
Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT) is a fully integrated, late-stage biotechnology company advancing a sustainable pipeline of investigational genetic therapies designed to correct the root cause of complex and rare disorders. Rocket's innovative multi-platform approach allows us to design the optimal gene therapy for each indication, creating potentially transformative options that enable people living with devastating rare diseases to experience long and full lives.

Rocket's adeno-associated viral (AAV) vector-based cardiovascular portfolio includes a late-stage clinical program for Danon Disease, a devastating heart failure condition resulting in thickening of the heart, and an early-stage clinical program for PKP2-arrhythmogenic cardiomyopathy (ACM), a life-threatening heart failure disease causing ventricular arrhythmias and sudden cardiac death. Rocket has also received IND clearance for its AAV-based gene therapy for BAG3-associated dilated cardiomyopathy (DCM), a heart failure condition that causes enlarged ventricles.

Rocket's lentiviral (LV) vector-based hematology portfolio consists of late-stage programs for Leukocyte Adhesion Deficiency-I (LAD-I), a severe pediatric genetic disorder that causes recurrent and life-threatening infections which are frequently fatal, Fanconi Anemia (FA), a difficult-to-treat genetic disease that leads to bone marrow failure (BMF) and potentially cancer, and Pyruvate Kinase Deficiency (PKD), a monogenic red blood cell disorder resulting in increased red cell destruction and mild to life-threatening anemia.

For more information about Rocket, please visit www.rocketpharma.com and follow us on LinkedIn, YouTube, and X.

Rocket Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements concerning Rocket's future expectations, plans and prospects that involve risks and uncertainties, as well as assumptions that, if they do not materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this release are forward-looking statements. You should not place reliance on these forward-looking statements, which often include words such as "could," "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. These forward-looking statements include, but are not limited to, statements concerning expectations regarding the safety and effectiveness of product candidates that Rocket is developing to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), Danon Disease (DD) and other diseases, 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, including the timing and outcome of the FDA's review of the additional CMC information that Rocket will provide in response to the FDA's request, the safety, effectiveness and timing of pre-clinical studies and clinical trials, Rocket's ability to establish key collaborations and vendor relationships for its product candidates, Rocket's ability to develop sales and marketing capabilities or enter into agreements with third parties to sell and market its product candidates, Rocket's ability to expand its pipeline to target additional indications that are compatible with its gene therapy technologies, Rocket's ability to transition to a commercial stage pharmaceutical company, and Rocket's expectation that its cash, cash equivalents and investments will be sufficient to fund its operations into the second quarter of 2027. 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 dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, unexpected expenditures, Rocket's competitors' activities, including decisions as to the timing of competing product launches, pricing and discounting, Rocket's ability to develop, acquire and advance product candidates into, enroll a sufficient number of patients into, and successfully complete, clinical studies, the integration of new executive team members and the effectiveness of the newly configured corporate leadership team, Rocket's ability to acquire additional businesses, form strategic alliances or create joint ventures and its ability to realize the benefit of such acquisitions, alliances or joint ventures, Rocket's ability to obtain and enforce patents to protect its product candidates, and its ability to successfully defend against unforeseen third-party infringement claims, 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, 2024, filed February 27, 2025 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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Investors
Meg Dodge
mdodge@rocketpharma.com

Media
Kevin Giordano
media@rocketpharma.com

Source: Rocket Pharmaceuticals, Inc.