# Rocket Pharmaceuticals Announces Positive Updates from Phase 1 Clinical Trial of RP-A501 in Danon Disease

November 15, 2021

*—Results demonstrate sustained benefit across clinical, functional and biomarker endpoints in all four patients with long-term follow up—*

*—NYHA class improvement (from II to I) in all three patients (two low-dose, one high-dose) with closely monitored immunosuppressive regimen—*

*—Decreased cardiac wall thickness with improved or stabilized ejection fraction on echocardiogram in all three patients with closely monitored immunosuppressive regimen—*

*— Sustained improvement or stabilization in BNP and 6-minute walk test across four patients—*

*—Sustained cardiac LAMP2B expression greater than 50% by immunohistochemistry and improved cardiac tissue architecture in all three patients with closely monitored immunosuppressive regimen—*

*—RP-A501 generally well tolerated at low-dose with manageable safety profile—*

*—Webcast to be held at 8:30 a.m. ET today—*

CRANBURY, N.J.--(BUSINESS WIRE)--Nov. 15, 2021-- Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT), a clinical-stage company advancing an integrated and sustainable pipeline of genetic therapies for rare childhood disorders, today announces updated data from the Phase 1 clinical trial evaluating a single intravenous infusion of RP-A501, the Company's investigational gene therapy, for the treatment of Danon Disease. This update, which includes interim safety and efficacy data from patients in the low-dose (6.7e13 vg/kg; n=3) and high-dose (1.1e14 vg/kg; n=2) adult and adolescent cohorts, demonstrates RP-A501 was generally well tolerated at the low-dose and conferred sustained clinical benefit.

"We are excited to announce positive data from our RP-A501 trial for Danon Disease showing clinical, functional and biomarker improvements at one year or beyond and potential early separation from the natural course of disease in adult and adolescent patients," said Gaurav Shah, M.D., Chief Executive Officer of Rocket Pharma. "Male patients living with Danon Disease suffer a heavy disease burden and face rapidly progressive heart failure in their teenage years. In this setting, even stabilization is highly beneficial, and clinical improvements as seen in our trial could be transformative and represent a step forward for the treatment of monogenic heart failure and gene therapy for cardiac diseases. We have initiated treatment in the pediatric cohort at the low-dose and anticipate moving as rapidly as possible toward Phase 2."

Dr. Barry Greenberg, Director of the Advanced Heart Failure Treatment Program at UC San Diego Health, Professor of Medicine at UC San Diego School of Medicine, and the principal investigator of the RP-A501 clinical study, is presenting a subset of the data at the American Heart Association (AHA) Scientific Sessions 2021. Dr. Greenberg added, "I am very encouraged by the ability to safely administer RP-A501 and show robust gene expression in the hearts of these young male patients with this devasting monogenic disorder. The clinical data to date also demonstrate encouraging results including clinical stabilization of this rapidly progressive disease."

**Safety Results**

- RP-A501 was generally well tolerated at the 6.7e13 vg/kg dose level. All observed adverse effects were reversible with no lasting sequelae. Early transaminase and creatinine kinase elevations returned to baseline or decreased.
- As previously disclosed, RP-A501 r-AAV dose-dependent toxicity was seen in one of the two patients treated at the 1.1e14 vg/kg dose level. The affected patient, who received the largest total dose, developed thrombotic microangiopathy (TMA) that fully resolved with supportive treatment including transient hemodialysis.
- Across both dose levels, the most common serious adverse event (SAE) observed was steroid-induced myopathy in three patients (two low-dose and one high-dose) which resolved subsequent to corticosteroid discontinuation.
- Based on the observed safety and efficacy to-date, the Company will focus on the low-dose cohort moving forward and will no longer administer the high-dose to study patients.
- An updated protocol developed in collaboration with the FDA has been implemented to mitigate development of TMA and

other treatment-related adverse events.

**Clinical and Biomarker Results for Patients With at Least 12 Months Follow-Up**

- **NYHA class:** An improvement in NYHA class (from II to I) was observed in three patients (two low-dose and one high-dose) who had closely monitored immunosuppression with follow-up greater than one year and stabilization was observed in one low-dose patient without a closely monitored immunosuppressive regimen.
- **BNP:** A substantial improvement in B-type natriuretic peptide (BNP), a key marker of heart failure, was observed in all three low-dose patients and one high-dose patient. Among the three low-dose patients, BNP decreased from a pretreatment baseline by 57% at 24 months, 79% at 18 months, and 75% at 15 months, respectively. In the high-dose patient, BNP decreased from a pretreatment baseline by 67% at 12 months.
- **LV wall thickness and ejection fraction:** In patients with closely monitored immunosuppression (two low-dose and one high-dose) left ventricular (LV) posterior wall thickness improved (average 23% decrease compared to pretreatment baseline) and ejection fraction improved or stabilized (average 20% increase compared to pretreatment baseline) at 12 to 18 months on echocardiography. Severe and progressive wall thickening is a hallmark of the hypertrophic cardiomyopathy of Danon Disease and is a major contributor to early mortality in male patients.
- **Cardiac output and diastolic dysfunction:** Cardiac output remained normal for all patients with improved or stable left heart filling pressures as measured by cardiac catheterization.
- **6MWT:** Three low-dose patients and one high-dose patient demonstrated improvements in the 6-minute walk test (6MWT). One low-dose patient improved from a pretreatment baseline of 443 meters (m) to 467 m at 24 months. The second low-dose patient improved from a pretreatment baseline of 405 m to 410 m at 18 months. The third low-dose patient improved from a pretreatment baseline of 427 m to 435 m at 15 months. The high-dose patient improved from a pretreatment baseline of 436 m to 492 m at 12 months.
- **Gene expression:** Evidence of sustained cardiac *LAMP2B* gene expression by immunohistochemistry and Western blot with qualitative improvement of vacuoles and cardiac tissue architecture on electron microscopy was observed at both dose levels. Sustained cardiac *LAMP2B* gene expression by immunohistochemistry was observed in all three patients with a closely monitored immunosuppressive regimen. Specifically, *LAMP2B* gene expression by immunohistochemistry in the low-dose (6.7e13 vg/kg) was 68% in one patient at Month 12 and 92% in another patient at Month 9. In one patient who received the high-dose (1.1e14 vg/kg), *LAMP2B* gene expression by immunohistochemistry was 100% at Month 12.

**Explanted Heart**

- As previously disclosed, one patient in the high-dose cohort underwent a heart transplant at Month 5. This patient had advanced disease including diminished LV ejection fraction (35%) on echocardiogram and markedly elevated LV filling pressure prior to treatment. His clinical course was characteristic of Danon Disease progression.
- Analysis of the explanted heart revealed significant fibrosis consistent with advanced Danon Disease.
- Myocardial tissue from the explanted heart at 5 months post-treatment displayed 100% LAMP2B protein expression by immunohistochemistry throughout non-fibrotic cardiac regions including the ventricles and other essential targeted areas.

**Webcast Details**

Rocket will host a conference call and webcast today at 8:30 a.m. ET to discuss the RP-A501 data in Danon Disease. Investors may access the conference call by dialing (866) 939-3921 from locations in the United States or +1 (678) 302-3550 from outside the United States. Please refer to conference ID number 50255994. A live webcast of the call can be accessed under “Events” in the Investors section of the Company’s website at https://ir.rocketpharma.com/. The webcast replay will be available on the Rocket website following the completion of the call.

**About RP-A501**

RP-A501 is an investigational gene therapy product being developed for Danon Disease and the first potential gene therapy for monogenic heart failure. It consists of a recombinant adeno-associated serotype 9 (AAV9) capsid containing a functional version of the human *LAMP2B* transgene (AAV9.*LAMP2B*). RP-A501 is currently being evaluated in a Phase 1 clinical trial, from which preliminary data of the low-dose cohort showed it was generally well tolerated and provided evidence of improved cardiac 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 are no specific therapies available for the treatment of Danon Disease.

**About Rocket Pharmaceuticals, Inc.**

Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT) is advancing an integrated and sustainable pipeline of genetic therapies that 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, Pyruvate Kinase Deficiency (PKD), a rare, monogenic red blood cell disorder resulting in increased red cell destruction and mild to life-threatening anemia, and Infantile Malignant Osteopetrosis (IMO), a bone marrow-derived disorder. Rocket's first clinical program using adeno-associated virus (AAV)-based gene therapy is for Danon Disease, a devastating, pediatric heart failure condition. 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 potential for RP-A501 to treat Danon Disease, Rocket's expectations regarding its guidance for 2021 in light of COVID-19, the safety and effectiveness of RP-A501, the expected timing and data readouts of Rocket's ongoing and planned clinical trials, Rocket's plans for the advancement of its Danon Disease program following the lifting of the FDA's clinical hold and additional data announcement 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, our expectations regarding the delays and impact of COVID-19 on clinical sites, 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, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, and 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, 2020, filed March 1, 2021 with the SEC. 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20211115005497/en/

**Media**
Kevin Giordano
Director, Corporate Communications
kgiordano@rocketpharma.com

**Investors**
Mayur Kasetty, M.D., M.B.A.
Director, Business Development & Operations
investors@rocketpharma.com

Source: Rocket Pharmaceuticals, Inc.