Rocket Pharmaceuticals Announces Positive Gene Expression, Clinical Biomarker and Preliminary Functional Data from Phase 1 Trial of RP-A501 for the Treatment of Danon Disease

December 8, 2020

—Low Dose Showed Positive Increases in Cardiac Protein Expression—Two Patients With >50% by IHC, One at Month 9 and One at Month 12–

—Decreases in Cardiac Biomarker BNP of >50% and Stabilization of Clinical Biomarkers CK-MB and Transaminases in Two Patients—

—Visible Reduction of Autophagic Vacuoles, a Primary Hallmark of Danon Disease, in Heart Muscle—

—Individual 1.62- and 1.35-Fold Increases in Cardiac Output Observed in Two Patients at Month 12 and Month 9, Respectively—

— Low Dose Cohort Generally Well-Tolerated with Manageable Safety—

—Safety Assessment in Two Adult Patients Treated in Higher Dose Cohort Ongoing with One Drug Product Related Serious Adverse Event Which Resolved Following Intensified Immunosuppressive Therapy—

—Webcast and Conference Call to be Held at 4:15 PM EST Today—

NEW YORK--(BUSINESS WIRE)--Dec. 8, 2020-- Rocket Pharmaceuticals, Inc. (NASDAQ: RCKT) (“Rocket”), a clinical-stage company advancing an integrated and sustainable pipeline of genetic therapies for rare childhood disorders, today announces preliminary data from its open-label, Phase 1 clinical trial of RP-A501, the Company’s adeno-associated viral vector (AAV)-based gene therapy candidate expressing LAMP2B for the treatment of Danon Disease. Danon Disease is a rare X-linked inherited disorder caused by genetic mutations in the *LAMP2* gene resulting in accumulation of autophagosomes and glycogen, particularly in cardiac muscle and other tissues, which ultimately leads to severe and frequently fatal cardiomyopathy. Preliminary data from patients in the low dose RP-A501 cohort showed that the gene therapy was generally well tolerated and provided early evidence of clinical benefit.

“We are very excited to report encouraging safety and tolerability results for RP-A501, as well as increased gene expression, positive biomarkers and functional measures observed in the low-dose cohort of the study. Based on these early results, we believe that a low dose of RP-A501 has the potential to confer meaningful therapeutic benefit with an overall manageable safety profile. Further, the safety results observed in the low dose cohort enabled us to treat the first two patients in the higher dose cohort,” said Gaurav Shah, M.D., Chief Executive Officer and President of Rocket.

“Cardiac *LAMP2B* protein expression by immunohistochemical staining was greater than 50% of normal *LAMP2B* in two patients with follow-up data of up to one year; these levels far exceeded the threshold estimated in females who largely do not develop heart failure until several decades later than males. In addition, RP-A501 demonstrated reduction of myocardial cell disarray and accumulation of autophagic vacuoles, a hallmark of Danon Disease. This translated into early stabilization and suggests a trend toward improvement in functional measures. Males with Danon Disease typically have elevated BNP, transaminases and creatine kinase as a result of skeletal and heart muscle damage. Cardiac dysfunction is often rapidly progressive and severe, with concomitant reductions in cardiac output. RP-A501 demonstrated consistent stabilization or improvements across all of these clinical measures as of the data cutoff. These early results suggest a path to a potentially transformative option for Danon Disease, and possibly the first viable gene therapy approach for cardiac diseases.”

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 added, “Children with Danon Disease live with a heavy disease burden. Young boys are often severely afflicted. They show evidence of early onset skeletal muscle weakness and heart disease that can progress rapidly to end-stage with death occurring on the average before age 20. A heart transplant can be performed, but is not curative and is associated with its own significant problems. The results-to-date for this first investigational gene therapy for monogenic heart failure show the potential for direct clinical benefit without emergence of unanticipated side effects of therapy.”

Preliminary safety and efficacy results from the three patients treated with the low dose of 6.7×10^{13} genome copies (gc)/kilogram (kg) and early safety information from the two patients treated with the higher dose of 1.1×10^{14} gc/kg as of November 2020 are as follows:

Safety Results

- RP-A501 showed a manageable safety profile in the three patients treated in the low dose cohort. No unexpected drug product related adverse events (AEs) or severe adverse events (SAEs) were observed. The most common adverse events were mild and were consistent with AEs caused by elevated transaminases observed post treatment. Elevation in transaminases were observed in all three low-dose patients and returned to baseline within the first one to two months post-treatment. These elevations were largely responsive to corticosteroids and other immunosuppressive therapies. All patients were given oral steroids to prevent or minimize potential immune-related events. At dose escalation, rituximab and tacrolimus were also added to the protocol as additional options to mitigate the immune response associated with RP-A501.
- Upon dose escalation to 1.1×10^{14} gc/kg, one of the two treated patients, who received the highest total dose volume of AAV9 and had some degree of pre-existing anti-AAV9 immunity, experienced a non-persistent, immune-related event that was classified as a drug product related SAE. Rocket believes this event was likely due to complement activation, resulting in reversible thrombocytopenia and acute kidney injury requiring transient hemodialysis. This patient returned to baseline within three weeks and regained normal kidney function.

Gene Expression Results

- All three low dose participants demonstrated evidence of cardiac *LAMP2B* expression by Western blot and/or immunohistochemistry.
- The two patients in the low dose cohort who had closely monitored compliance with the immunosuppressive regimen showed high levels of cardiac *LAMP2B* expression along with clinical biomarker improvements. In cardiac biopsies of patients treated at a systemic dose of $6.7x10^{13}$ gc/kg, *LAMP2B* gene expression was observed to be present in 68% of cells versus normal as determined by immunohistochemistry at month 9 in one patient, and at 92% of cells versus normal at month 12 in the other patient. Western blot assessment showed 61% of normal *LAMP2B* protein expression at month 9 in one patient. The 12-month Western blot data were still pending for all three patients as of the data cutoff.

Biomarker Results

- Two of the three low dose patients demonstrated key clinical biomarker improvements consistent with improved cardiac function. Brain natriuretic peptide (BNP), a key marker of heart failure, improved in all three patients, including greater than 50% in the two patients with closely monitored immunosuppressive regimen compliance. Additionally, creatine kinase myocardial band (CPK-MB) either improved or stabilized in these two patients. Notably, all three patients showed visible improvements in autophagic vacuoles, a hallmark of Danon Disease pathology, as assessed by electron microscopy.
- Two of the three low dose patients with closely monitored immunosuppressive regimen compliance demonstrated improvement in cardiac output as measured by invasive hemodynamics, including one patient who showed a 1.62-fold increase in cardiac output at month 12, and one patient who showed a 1.35-fold increase at month 9.

The non-randomized, open-label Phase 1 trial was designed to enroll both pediatric and young adult male patients in escalating dose cohorts. Following the review of safety data from the first young adult cohort, all subsequent cohorts will include 2-4 patients per cohort. The study is designed to assess the safety and tolerability of a single intravenous (IV) infusion of RP-A501. Additional outcome measures include cardiomyocyte and skeletal muscle transduction by gene expression, histologic correction via endomyocardial biopsy and clinical stabilization via cardiac imaging and functional cardiopulmonary testing. Further information about the clinical program is available here.

Conference Call Details

Rocket management will host a conference call and webcast on December 8, at 4:15 PM EST. To access the call and webcast, please click here. The webcast replay will be available on the Rocket website following the completion of the call.

Investors may listen to the 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 50040516.

About Danon Disease

Danon Disease is caused by mutations in the gene encoding lysosome-associated membrane protein 2 (LAMP-2), an important mediator of autophagy. It is estimated to have a prevalence of 15,000 to 30,000 patients in the U.S. and the European Union. The disease is often fatal in male patients in the second or third decade of life due to rapidly progressive heart failure. Available therapies for Danon Disease include 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) (“Rocket”) 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 its guidance for 2020 in light of COVID-19, the safety, effectiveness and timing of product candidates that Rocket may develop, to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), Infantile Malignant Osteopetrosis (IMO) and Danon Disease, 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed November 6, 2020 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.

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Source: Rocket Pharmaceuticals, Inc.