Rocket Pharmaceuticals Announces FDA Clearance of IND for Clinical Trial of RP-A601 for PKP2 Arrhythmogenic Cardiomyopathy (ACM)

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First clinical gene therapy program for PKP2-ACM, a devastating inherited heart disease affecting approximately 50,000 people in the U.S. and EU

Robust preclinical proof of concept studies showed RP-A601 decreased arrhythmias and increased survival in the PKP2 knockout mouse model

Initiating Phase 1 trial start-up activities and rapidly working towards first patient treatment

CRANBURY, N.J.--(BUSINESS WIRE)--May 9, 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 it has received clearance from the U.S. Food and Drug Administration (FDA) for the Company's Investigational New Drug (IND) application for RP-A601, an AAV.rh74-based gene therapy candidate for the treatment of arrhythmogenic cardiomyopathy due to plakophilin 2 pathogenic variants (PKP2-ACM) a devastating inherited heart disease that can lead to life-threatening arrhythmias, cardiac structural abnormalities, and sudden cardiac death. The current standard of care for patients with PKP2-ACM consists of medical therapy, implantable cardioverter defibrillators (ICDs), and ablations, which are not curative. Even with treatment, life-threatening arrhythmias and progression of disease may still occur. PKP2-ACM affects approximately 50,000 people in the U.S. and Europe.

"Today's news is a significant milestone, as we build on our leading cardiovascular gene therapy expertise to advance a historic second program targeting the heart into clinical development, this time for patients with PKP2-ACM who have an urgent need for improved treatment options," said Kinnari Patel, PharmD, MBA, President and Chief Operating Officer, Rocket Pharma. "RP-A601 offers the potential of a one-time, curative alternative to medical therapy, ICDs, and ablations which are associated with adverse effects, complications, and recurrence of arrhythmias and do not halt the progression of disease. Robust preclinical proof of concept has demonstrated decreased arrhythmias and increased survival. With IND clearance in hand, we are rapidly advancing the first investigational gene therapy for PKP2-ACM into the clinic."

The multi-center Phase 1, dose escalation trial will evaluate the safety and preliminary efficacy of RP-A601 in at least six adult PKP2-ACM patients with ICDs and overall high risk for arrhythmias. The study will assess the impact of RP-A601 on PKP2 myocardial protein expression, cardiac biomarkers, and clinical predictors of life-threatening ventricular arrhythmias and sudden cardiac death. Patients in the dose-escalation trial will receive a single dose of RP-A601. The starting dose will be 8×10^{13} GC/kg. The rh74 serotype used in RP-A601 was selected based on a favorable safety profile in gene therapy clinical development programs for other diseases and overall favorable benefit-risk profile in extensive preclinical RP-A601 studies.

RP-A601 Development Highlights

- A partnership between Rocket and leading scientific collaborators at NYU Grossman School of Medicine resulted in vigorous and translationally relevant animal models and preclinical studies. These studies showed that RP-A601 decreased arrhythmias, improved right ventricular morphology and function, and increased survival in PKP2 knockout mice. Scientific collaborators include Mario Delmar, M.D., Ph.D., Patricia and Robert Martinsen Professor of Cardiology and Marina Cerrone, M.D., Research Associate Professor, Co-Director, Inherited Arrhythmia Clinic.
- GMP drug product manufacturing has been completed, and a potency assay has been both developed and qualified.
- A robust clinical protocol has been developed, vetted by an advisory board comprised of experts in PKP2-ACM and gene therapy clinical development and informed by insights from the patient community.
- Natural history studies are planned to provide additional context for the Phase 1 trial.
- Initial clinical sites for the Phase 1 trial have been selected. Principal Investigators include Barry Greenberg, M.D., FHFSA, Director of the Advanced Heart Failure Treatment Program at University of California, San Diego Medical Center and Joseph Rossano, M.D., M.S., FAAP, FACC, Co-Director of the Cardiac Center and Chief of the Division of Cardiology at Children's Hospital of Philadelphia.
- Rocket is initiating Phase 1 study start-up activities and rapidly working towards first patient treatment.

Preclinical data from the RP-A601 program will be presented as a late-breaking abstract at the 26th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT) on Friday, May 19, 2023, 8:00 a.m. – 9:45 a.m. PT. More information can be found here.

About PKP2-Arrhythmogenic Cardiomyopathy (PKP2-ACM)

PKP2-ACM is an inherited heart disease caused by mutations in the *PKP2* gene and characterized by life-threatening ventricular arrhythmias, cardiac structural abnormalities, and sudden cardiac death. PKP2-ACM affects approximately 50,000 adults and children in the U.S. and Europe. Patients living with PKP2-ACM have an urgent unmet medical need, as current medical, implantable cardioverter defibrillator (ICD), and ablation therapies do not consistently prevent disease progression or arrhythmia recurrence, are associated with significant morbidity including inappropriate shocks and device and procedure-related complications, and do not address the underlying pathophysiology or genetic mutation. RP-A601 is being investigated as a one-time, potentially curative gene therapy treatment that may improve survival and quality of life for patients affected by this devastating 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 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 (LV) 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 preclinical AAV-based gene therapy programs in PKP2-arrhythmogenic cardiomyopathy (ACM) and 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 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, 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 "aim," "anticipate," "believe," "can," "continue," "design," "estimate," "expect," "intend," "may," "plan," "potential," "will give," "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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