



Precision BioSciences and SpringWorks Therapeutics Dose First Patient in Expanded Phase 1/2a Clinical Trial Evaluating PBCAR269A with Nirogacestat in Patients with Relapsed/Refractory Multiple Myeloma

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DURHAM, N.C. & STAMFORD, Conn.--(BUSINESS WIRE)--Jun. 28, 2021-- Precision BioSciences, Inc. (Nasdaq: DTIL), a clinical stage biotechnology company developing allogeneic CAR T and *in vivo* gene correction therapies with its ARCUS® genome editing platform, and SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a clinical-stage biopharmaceutical company focused on developing life-changing medicines for patients with severe rare diseases and cancer, today announced that the first patient has been dosed in the combination arm of Precision's Phase 1/2a trial evaluating PBCAR269A. In the study, Precision's investigational allogeneic BCMA-targeted CAR T cell therapy will be combined with nirogacestat, SpringWorks' investigational gamma secretase inhibitor (GSI), in patients with relapsed/refractory (R/R) multiple myeloma.

"We are pleased to begin dosing patients in the combination arm of our ongoing Phase 1/2a study evaluating PBCAR269A, our first-generation allogeneic CAR T candidate targeting BCMA in patients with R/R multiple myeloma. BCMA is a well-established therapeutic target for multiple myeloma and this arm of the study pairs PBCAR269A with SpringWorks' nirogacestat, a gamma secretase inhibitor, a combination intended to offer strong mechanistic rationale for clinical benefit," said Alan List, M.D., Chief Medical Officer at Precision BioSciences. "As we look forward to sharing interim monotherapy data for PBCAR269A later this year, we are also conducting IND enabling studies to advance PBCAR269B, an immune-evading, stealth cell formulation into the clinic in 2022. We have high conviction in both our technology and BCMA as a target and we are pursuing a broad, data-driven strategy to inform our future development plans for this indication."

"We are pleased to advance this combination into the clinic so we can evaluate if nirogacestat paired with PBCAR269A offers a safe and efficacious treatment option for patients with multiple myeloma," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "We have made significant progress in developing nirogacestat as a cornerstone of BCMA combination therapy across modalities and look forward to generating clinical data with all of our partners."

In September 2020, Precision and SpringWorks entered into a clinical collaboration in which Precision is sponsoring the expanded Phase 1/2a study of PBCAR269A to include nirogacestat and evaluate the safety and preliminary clinical activity of the combination therapy. Simultaneously, Precision continues to enroll patients in the highest dose cohort (Dose Level 3 at 6.0×10^6 cells/kg) in its monotherapy study with PBCAR269A.

About PBCAR269A (Clinical Trials Study Identifier: [NCT04171843](#))

PBCAR269A is an allogeneic BCMA-targeted CAR T cell therapy candidate being evaluated for safety and preliminary clinical activity in a Phase 1/2a multicenter, nonrandomized, open-label, parallel assignment, single-dose, dose-escalation, and dose-expansion study of adults with relapsed/refractory (R/R) multiple myeloma. The starting dose of PBCAR269A is 6×10^5 CAR T cells/kg body weight with subsequent cohorts receiving escalating doses to a maximum dose of 6×10^6 CAR T cells/kg body weight.

PBCAR269A is part of a pipeline of cell-phenotype optimized allogeneic CAR T therapies derived from healthy donors and then modified via a simultaneous TCR knock-out and CAR T knock-in step with the Company's proprietary ARCUS® genome editing technology. Precision BioSciences optimizes its CAR T therapy candidates for immune cell expansion in the body by maintaining a high proportion of naive and central memory CAR T cells.

The U.S. Food and Drug Administration (FDA) granted Fast Track Designation to PBCAR269A for the treatment of R/R multiple myeloma for which the FDA previously granted Orphan Drug Designation. The PBCAR269A clinical trial is being conducted at multiple U.S. sites.

About Nirogacestat

Nirogacestat is an investigational, oral, selective, small molecule gamma secretase inhibitor in Phase 3 clinical development for desmoid tumors, which are rare and often debilitating and disfiguring soft-tissue tumors. Gamma secretase cleaves multiple transmembrane protein complexes, including Notch, which is believed to play a role in activating pathways that contribute to desmoid tumor growth.

In addition, gamma secretase has been shown to directly cleave membrane-bound BCMA, resulting in the release of the BCMA extracellular domain, or ECD, from the cell surface. By inhibiting gamma secretase, membrane-bound BCMA can be preserved, increasing target density while reducing levels of soluble BCMA ECD, which may serve as decoy receptors for BCMA-directed therapies. Nirogacestat's ability to enhance the activity of BCMA-directed therapies has been observed in preclinical models of multiple myeloma. SpringWorks is evaluating nirogacestat as a BCMA potentiator and has six collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies and two bispecific antibodies. In addition, SpringWorks and Fred Hutchinson Cancer Research Center have entered into a sponsored research agreement to further characterize the ability of nirogacestat to modulate BCMA and potentiate BCMA directed therapies using a variety of preclinical and patient-derived multiple myeloma models developed by researchers at Fred Hutch.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors and from

the European Commission for the treatment of soft tissue sarcoma. The FDA also granted Fast Track and Breakthrough Therapy Designations for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis.

About Precision BioSciences, Inc.

Precision BioSciences, Inc. is a clinical stage biotechnology company dedicated to improving life (DTIL) with its wholly proprietary ARCUS® genome editing platform. ARCUS is a highly specific and versatile genome editing platform that was designed with therapeutic safety, delivery, and control in mind. Using ARCUS, the Company's pipeline consists of multiple "off-the-shelf" CAR T immunotherapy clinical candidates and several *in vivo* gene correction therapy candidates designed to cure genetic and infectious diseases where no adequate treatments exist. For more information about Precision BioSciences, please visit www.precisionbiosciences.com.

About SpringWorks Therapeutics

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for patients living with severe rare diseases and cancer. SpringWorks has a differentiated targeted oncology portfolio of small molecule product candidates and is advancing two potentially registrational clinical trials in rare tumor types as well as several other programs addressing highly prevalent, genetically defined cancers. SpringWorks' strategic approach and operational excellence in clinical development have enabled it to rapidly advance its two lead product candidates into late-stage clinical trials while simultaneously entering into multiple shared-value partnerships with innovators in industry and academia to expand its portfolio to create more solutions for patients with cancer. For more information, please visit www.springworkstx.com and follow @SpringWorksTx on [Twitter](#) and [LinkedIn](#).

Precision BioSciences Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the expected timing of clinical updates and interim data reports related to PBCAR269A in combination with nirogacestat, statements regarding our clinical development and research pipeline and the potential clinical benefit of our product candidates. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "believe," "could," "expect," "should," "plan," "intend," "estimate," "target," "mission," "goal," "may," "will," "would," "should," "could," "target," "potential," "project," "predict," "contemplate," "potential," or the negative thereof and similar words and expressions.

Forward-looking statements are based on management's current expectations, beliefs and assumptions and on information currently available to us. Such statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to become profitable; our ability to procure sufficient funding and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical or greenhouse studies and clinical or field trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields; our or our collaborators' ability to identify, develop and commercialize product candidates; pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators' development of product candidates; our or our collaborators' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; our or our collaborators' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators' ability to enroll patients; changes in interim "top-line" and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events effects of the outbreak of COVID-19, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2021, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at www.sec.gov and the Investors & Media page of our website at investor.precisionbiosciences.com. All forward-looking statements speak only as of the date of this press release and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

SpringWorks Therapeutics Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, and other future conditions. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks relating to: (i) the success and timing of our product development activities, including the initiation and completion of SpringWorks' clinical trials, (ii) the fact that interim data from a clinical study may not be predictive of the final results of such study or the results of other ongoing or future studies, (iii) the success and timing of our collaboration partners'

ongoing and planned clinical trials, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks' business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. For further information regarding the risks, uncertainties and other factors that may cause differences between SpringWorks' expectations and actual results, you should review the "Risk Factors" in Item 1A of Part I of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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