Provention Bio Provides Update on the Potential Timing of Teplizumab At-Risk Type 1 Diabetes (T1D) Biologics License Application (BLA) Resubmission

Data collection completed for PROTECT Pharmacokinetic/Pharmacodynamic (PK/PD) substudy

Company working with the U.S. FDA to finalize the design of population PK model to be used to analyze substudy data and plans to request a fourth quarter 2021 Type A meeting to obtain approval to proceed with unblinding

Company believes preliminary top-line study analysis of clinically relevant PD data are supportive of comparability, however, FDA will need to opine on the significance of these data

RED BANK, N.J., Sept. 13, 2021 /PRNewswire/ -- Provention Bio, Inc. (Nasdaq: PRVB), a biopharmaceutical company dedicated to intercepting and preventing immune-mediated disease, today provided an update on the status and timing of its ongoing efforts to address FDA considerations cited in the Complete Response Letter (CRL) issued to the Company by the FDA on July 2, 2021.

The Company has completed the collection of data from a PK/PD substudy in the ongoing PROTECT Phase 3 trial in newly diagnosed T1D patients (AGC Biologics N~30 patients, Eli Lilly N~130 patients) to determine comparability between the Company's planned commercial drug product and drug product originating from drug substance manufactured for historical trials of teplizumab. During ongoing informal discussions with the FDA to finalize and agree upon the design of the population PK model that will generate the PK parameters comparing drug products, the FDA has recommended that the Company request a formal Type A meeting and submit briefing documents related to the population PK model. The objective of this meeting with the FDA is to agree on the PK model's design prior to the Company populating the model with relevant PK data collected from the PROTECT substudy. The Company is working towards a request and submission to allow this Type A meeting to occur in the fourth quarter of this year.

Additionally, the Company disclosed preliminary PD marker information upon therapeutic dosing of teplizumab from the substudy data that the Company believes are supportive, although not determinative, of comparability between the two drug products. The FDA has not yet opined on these data or their significance, and the Company looks forward to discussing with the FDA. These PD markers include lymphocyte counts, CD3 receptor occupancy and T-cell activation.

The Company also recently completed a Type A meeting with the FDA to discuss several additional considerations related to product quality that were cited in the CRL. The Company continues to believe that the product quality CRL considerations have either already been addressed by prior amendments to the BLA or are addressable in the short term. As it relates to the deficiencies noted during the recent general inspection at a fill/finish facility used by the Company mentioned in the CRL, this facility's inspection has since been closed out by the FDA in August of 2021.

The Company has posted an update to its corporate slide presentation containing additional details pertaining to the information commented on within this press release. The presentation can be found at

www.proventionbio.com in the Investor's section.

"We believe we are making significant progress in our work to address the observations cited by the FDA in the CRL for teplizumab we received in July and we will continue to work with the sense of urgency that the patient community and our investors expect of us," said Ashleigh Palmer, co-founder and CEO of Provention Bio. "We are encouraged by our interactions with the FDA and look forward to finalizing, to the FDA's satisfaction, the design of the population PK model that will be used to further determine comparability, as well as evaluate the clinical relevance of the outputs. Additionally we are encouraged by the consistent incremental PD marker data that we are sharing today."

The Unmet Need in Type 1 Diabetes (T1D):

Over 1.6 million Americans have T1D, an autoimmune disease caused by the destruction of beta cells. Diagnosis of T1D usually occurs in children and young adults, but it can happen at any age after symptoms appear when a person cannot make enough insulin. However, T1D starts in the body long before any symptoms and can be detected through a blood test. The psychological impact of T1D is hard to quantify, but a diagnosis is life-altering, and regular monitoring and maintenance can be extremely stressful. T1D typically takes more than a decade off a person's life, and life expectancy is reduced by 16 years on average for people diagnosed before the age of 10. Insulin therapy and glucose monitoring are currently the standard of care for treating clinical-stage T1D, and are necessary to keep T1D patients alive. The constant monitoring and administration of insulin represents a significant life-long burden for patients. No disease-modifying treatments for T1D are currently available.

About Teplizumab (PRV-031):

Teplizumab is an investigational anti-CD3 monoclonal antibody (mAb) being developed for the delay of clinical type 1 diabetes (T1D) in at-risk individuals. In the pivotal TN-10 Study, a single 14-day course of teplizumab delayed insulin-dependent, clinical-stage disease by a median of at least two years in presymptomatic patients with Stage 2 T1D compared to placebo. The observed adverse events were mechanism-based, transient, and predictable, including lymphopenia, transaminase elevations, rash, and cytokine release events. These results were published in the *New England Journal of Medicine* and simultaneously presented at the American Diabetes Association meeting in 2019. More than 800 patients have received teplizumab in multiple clinical studies involving more than 1,000 subjects. In previous studies of newly diagnosed patients, teplizumab consistently demonstrated the ability to preserve beta-cell function as shown by C-peptide, a measure of endogenous insulin production. It correspondingly reduced the need for insulin use. Teplizumab has been granted Breakthrough Therapy Designation by the FDA and PRIME designation by the European Medicines Administration. Provention is currently also evaluating teplizumab in patients with newly diagnosed insulin-dependent T1D (the Phase 3 PROTECT study).

About Provention Bio, Inc.:

Provention Bio, Inc. (Nasdaq: PRVB) is a biopharmaceutical company focused on advancing the development of investigational therapies that may intercept and prevent debilitating and life-threatening immune-mediated disease. The Company's pipeline includes clinical-stage product candidates that have demonstrated in pre-clinical or clinical studies proof-of-mechanism and/or proof-of-concept in autoimmune diseases, including type 1 diabetes, celiac disease and lupus. Visit www.ProventionBio.com for more information and follow us on Twitter: @ProventionBio.

Internet Posting of Information:

Provention Bio, Inc. uses its website, www.proventionbio.com, as a means of disclosing material nonpublic

information and for complying with its disclosure obligations under Regulation F.D. Such disclosures will be included on the Company's website in the "News" section. Accordingly, investors should monitor this portion of the Company's website, in addition to following its press releases, SEC filings and public conference calls and webcasts.

Forward-Looking Statements:

Certain statements in this press release are forward-looking, including but not limited to, statements relating to the medical need in T1D at-risk patients, the potential therapeutic effects and safety of teplizumab in at-risk T1D patients, the potential for PK/PD substudy data and analyses to address the FDA's PK comparability considerations, the Company's belief that the remaining product quality issues cited in the CRL are addressed or may be adressable in the short-term, the timing of the FDA's review of such data and analyses if submitted by the Company and the Company's plans to address the other matters raised in the CRL. These statements may be identified by the use of forward-looking words such as "will," "believe," and "may," among others. These forward-looking statements are based on the Company's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to FDA disagreeing with the Company's interpretation of data and analysis, including the preliminiary PD data referenced in this release which could change as these data are finalized; delays in or failure to obtain FDA approvals for teplizumab or other Company product candidates and the potential for noncompliance with FDA regulations; any inability to successfully work with FDA to find a satisfactory solution to address its concerns in a timely manner or at all, including any inability to provide the FDA with PK/PD data from our ongoing Phase 3 PROTECT study or other data sufficient to support an approval of the BLA for teplizumab; an inability to satisfactorily address other matters cited in the CRL including relating to product quality, the safety update required by FDA or any other FDA requirements for an approval of teplizumab; the potential impacts of COVID-19 on our business and financial results; changes in law, regulations, or interpretations and enforcement of regulatory guidance; uncertainties of patent protection and litigation; the Company's dependence upon third parties; substantial competition; the Company's need for additional financing and the risks listed under "Risk Factors" in the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2021 and any subsequent filings with the Securities and Exchange Commission. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Provention does not undertake an obligation to update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by applicable law. The information set forth herein speaks only as of the date hereof.

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