Provention Bio Provides Additional Regulatory Update on Biologics License Application for Teplizumab for the Delay or Prevention of Clinical Type 1 Diabetes in At-Risk Individuals

RED BANK, N.J., April 27, 2021 /PRNewswire/ -- Provention Bio, Inc., (Nasdaq: PRVB), a biopharmaceutical company dedicated to intercepting and preventing immune-mediated disease, today announced the Company took part in an informal meeting with the U.S. Food and Drug Administration (FDA) on April 23, 2021, in connection with the FDA's ongoing review of the teplizumab Biologic License Application (BLA) for the delay or prevention of clinical type 1 diabetes (T1D). The purpose of this meeting was to discuss the FDA's considerations, thus far, regarding comparability between the Company's proposed commercial product and drug product used historically in clinical trials originating from drug substance manufactured by Eli Lilly over a decade ago.

The FDA reported at the meeting that it had concluded that the pharmacokinetic (PK) profiles of the two drug products evaluated in the Company's single, low-dose pharmacokinetic/pharmacodynamic (PK/PD) bridging study conducted in healthy volunteers are not comparable, since the intended commercial product did not meet the pre-specified 80-125% PK area under the curve (AUC) comparability target range. The FDA also stated that it cannot be certain if this observation is not clinically relevant, given that the relationship between transient lymphocyte reduction, a PD marker, which was comparable in the PK/PD bridging study, and clinical efficacy, has yet to be fully validated.

The FDA emphasized its understanding of the high unmet need associated with delaying the onset of clinical-stage T1D and reiterated their willingness to work with the Company to find a solution and path forward for the comparability issue. Nevertheless, the Company is reiterating previous guidance that the FDA's PK comparability considerations are likely to result in a delay in potential BLA approval timelines and that the specifics of such delay will depend upon the outcome of ongoing discussions with the FDA to find a solution, including potentially providing FDA reviewers with PK/PD data from the Company's on-going Phase 3 PROTECT study in newly diagnosed patients.

The FDA also informed the Company that it plans to mention its PK comparability review in the clinical pharmacology summary of its briefing materials for the Advisory Committee meeting on May 27th, along with a statement that the FDA is actively working with the Company to resolve the issue and that the focus of the Advisory Committee meeting is efficacy and safety of teplizumab. It is the Company's understanding that since the FDA's PK comparability considerations do not bear on the benefit-risk assessment of the TN-10 study clinical data package, no comparability related questions or discussion topics are planned for the meeting. The FDA also recommended that both the FDA and the Company update their Advisory Committee briefing materials to reflect the removal of the term "prevention" from the previously proposed indication, as the remaining term "delay" more accurately reflects the results of the TN-10 trial.

"We would like to thank the FDA for meeting with us to explain its PK comparability considerations, thus far, and especially for its willingness to work with us to find a path forward," stated Ashleigh Palmer, CEO and Co-Founder, Provention Bio. "We are also fully aligned with the FDA's recommendation to remove the term 'prevention' from the wording of teplizumab's initial indication and instead focus exclusively on delaying the progression of disease. We believe this will help to reinforce the fact that, while pre-symptomatic, T1D patients with two autoantibodies and dysglycemia already have the disease and may benefit from therapeutic options targeting the preservation of functional beta cell mass. We remain enthusiastic about the clinical efficacy and safety data submitted in connection with the BLA in support of teplizumab's potential to address the high unmet needs of pre-symptomatic T1D patients. Finally, we are looking forward to participating alongside the patient community, treating physicians, and additional members of the T1D community in the upcoming FDA Advisory Committee Meeting, the importance of which could not be more clear at this juncture."

About Teplizumab (PRV-031):
Teplizumab is an investigational anti-CD3 monoclonal antibody (mAb) with a filed BLA under Priority Review by the FDA for the delay or prevention of clinical type 1 diabetes (T1D) in at-risk individuals. 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, a measure of endogenous insulin production. It correspondingly reduced the need for exogenous

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 diseases. The Biologics License Application (BLA) for teplizumab, its lead investigational drug candidate, for the delay or prevention of clinical type 1 diabetes in at-risk individuals has been filed by the U.S. Food and Drug Administration (FDA). The Company's pipeline includes additional clinical-stage product candidates that have demonstrated in pre-clinical or clinical studies proof-of-mechanism and/or proof-of-concept in other autoimmune diseases, including 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 regulatory review of the BLA submission for teplizumaband the potential approval of teplizumab, including a delay relating to the same, the potential therapeutic effects and safety of teplizumab and the FDA's willingness to work with us to find a solution to the teplizumab comparability issue between our proposed commercial product and drug product used historically in clinical trials originating from drug substance manufactured by Eli Lilly, including potentially providing FDA reviewers with PK/PD data from the our on-going Phase 3 PROTECT study in newly diagnosed patients. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," 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 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 the our on-going Phase 3 PROTECT study or other data sufficient to support an approval of the BLA for 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 annual report on Form 10-K for the year ended December 31, 2020, 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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