Press Release

Teon Therapeutics Announces FDA Acceptance of IND Application for Novel, Oral Immune Checkpoint Inhibitor, TT-816

- First-in-class, oral cannabinoid CB_2 antagonist acting as an immune checkpoint inhibitor has potential to enhance immune response to treat solid tumors -

- Company on track to initiate Phase 1/2 clinical trial in third quarter 2022 -

SAN FRANCISCO, June 1, 2022 – Teon Therapeutics (Teon), a clinical-stage biopharmaceutical company targeting metabolic signaling pathways and pioneering the development of G-Protein Coupled Receptor (GPCR) immuno-oncology therapies in difficult-to-treat cancers, today announced the acceptance by the U.S. Food and Drug Administration (FDA) of Teon's Investigational New Drug (IND) application for the study of TT-816. TT-816 is a novel, oral cannabinoid CB_2 receptor antagonist acting as an immune checkpoint inhibitor for the treatment of a broad range of solid tumors. The IND enables Teon to initiate its planned Phase 1/2 clinical trial designed to assess the dosing, tolerability and safety of TT-816 in patients with advanced cancers as a monotherapy and in combination with existing standard of care anti-PD-1 checkpoint inhibitors.

"The FDA's acceptance of the IND for TT-816 is an important validation of our approach to targeting a novel immune checkpoint pathway and marks a significant milestone for Teon," said Serge Messerlian, Chief Executive Officer of Teon. "As a highly-selective orally-administered checkpoint inhibitor, we believe that TT-816 has the promise to change the treatment landscape in many difficult-to-treat cancers, including lung, renal, and ovarian, and we are very pleased to begin evaluating its potential in the clinic."

The cannabinoid CB_2 receptor belongs to the G protein-coupled receptor family. The cannabinoid CB_2 receptor, selectively targeted by TT-816, is a peripheral receptor found predominantly in the immune system and regulates inflammation and the immune response. Elevated CB_2 receptor expression is associated with worse overall survival[1-5] and aggressiveness of cancer.[6,7] Research has shown that CB_2 receptor activation does not have any psychoactive properties unlike CB_1 receptors which are located primarily in the brain.[8]

Preclinical results indicate that TT-816 enhances both the effect of NK cell tumor killing and T cell activation *in vitro* and increases both tumor infiltrating T cells and NK cells *in*

vivo. TT-816 dose-dependently inhibits tumor growth in animal models, has an additive effect with anti-PD-1 in the 'hot' tumor model and acts synergistically with anti-PD-1 in the 'cold' tumor model where the anti-PD-1 alone had no effect.

"TT-816 is a novel immune checkpoint inhibitor that has demonstrated that it may have the potential to enhance both innate and adaptive immunity, synergize antitumor effects with current immune checkpoint inhibitor therapies and directly promote immune cell penetration into solid tumors," said Lina Yao, MD, PhD, Chief Scientific Officer of Teon. "TT-816 adds to Teon's strong portfolio of highly-selective small molecules furthering the Company's aim to advance first- or best-in-class cancer immunotherapies to patients."

Initiation of the Phase 1/2 TT-816 clinical trial is on track for third quarter 2022.

About TT-816

TT-816 is a first-in-class, oral cannabinoid CB_2 receptor antagonist acting as an immune checkpoint inhibitor and is highly selective for the CB_2 receptor versus the CB_1 receptor. By inhibiting the actions of the CB_2 receptors found in many difficult-to-treat cancers, including lung, renal, and ovarian, TT-816 has the potential to enhance immune response to treat solid tumors.

Targeting GPCR for Oncology – Tomorrow's Treatments

With more than 700 approved drugs currently directed at them, GPCRs are the most commonly utilized target in today's treatment paradigm, however, their potential in oncology and moreover, immuno-oncology, has yet to be leveraged. GPCRs control a broad range of cellular processes vital to the formation and progression of tumors. Small molecules are the most prevalent modulators of GPCR-targeted therapies. Insights into the roles of GPCRs in the tumor microenvironment and how they modulate both tumor-generating signal transduction pathways as well as interactions with immune system defense mechanisms may allow the pursuit of more novel GPCR-directed therapies.

About Teon Therapeutics

Teon Therapeutics is a clinical-stage biopharmaceutical company dedicated to improving the lives of cancer patients by developing a focused portfolio of oral, GPCR-targeted small molecules that inhibit immunosuppressive and cancer-promoting signaling pathways in difficult-to-treat cancers. Teon's rich pipeline includes adenosine pathway inhibitors as well as a small molecule, cannabinoid CB_2 receptor antagonist acting as an immune checkpoint inhibitor. Teon initiated a Phase1/2 trial with its lead program, TT-702, an A_2B receptor-specific antagonist, in 2021 and expects to initiate a Phase 1/2 trial for TT-816, a

cannabinoid CB_2 antagonist in the third quarter 2022. The highly accomplished scientific leadership team are experts in tumor metabolism, cell signaling and GPCR therapeutic design. Teon completed its $30M Series A financing round in February 2021. For more information about Teon Therapeutics, please visit: www.teontherapeutics.com.

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