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ENB Therapeutics Presents Top-line Results from Phase 1b ENBOLDEN-101 Study in Solid Tumors Refractory to Standard of Care at the Immuno-oncology Summit 2023

ENB is developing first in class small molecule ENB-003 to selectively targeting the ETB receptor - a novel immune checkpoint

- The ENB-003 in combination with KEYTRUDA® (pembrolizumab) was well tolerated
- Promising preliminary efficacy signals with 33% disease control rate (DCR) across all cohorts
- Efficacy appears to correlate with endothelin B receptor (ETBR) expression: 83% DCR in ETBR-Hi patients in cohort 6 (RP2D)
- Platinum refractory/ resistant microsatellite stable ovarian cancer patients with 80% DCR across all cohorts

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NEW YORK--(BUSINESS WIRE)--ENB Therapeutics, Inc., a biotechnology company pioneering a new and differentiated class of therapeutics targeting the endothelin B receptor (ETBR) inhibitor, today announced that the company has completed enrollment of its international Phase 1 ENBOLDEN-101 trial investigating the safety and efficacy of lead product ENB-003 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy. The Phase ½a study is a multicenter, open-label study conducted in the US and Australia and is comprised of two parts. Part 1 recruited 46 patients and was a dose-escalation study to determine the recommended dose for the Part 2 expansion phase of the study. The results of this study will be presented by ENB Therapeutics in a poster titled, "ENB-003, an ETBR antagonist, in combination with pembrolizumab for refractory advanced solid tumors: Topline data from the ENBolden-101 Phase 1B study" at the Immuno-oncology Summit which is being held August 7-9, 2023 in Boston, Massachusetts.

ENB-003 in combination with pembrolizumab was well tolerated in the dose escalation study and demonstrated no DLTs across the 6 dosing cohorts. The most common treatment emergent adverse events irrespective of grade or causality included fatigue (28.2%), constipation (26.1%), abdominal pain (26.1%), nausea (23.9%), anemia 17.4%, diarrhea (17.4%). Serious adverse events, grade 3 and above considered possibly related to study treatment included fatigue (n=4), diarrhea (n=3), dyspnea (n=3) constipation (n=2), rash (n=2). 15 patients with evaluable disease were enrolled in cohorts 1-5 (ENB-003 dose range 150ug-1000ug) and 15 patients with evaluable disease were enrolled in the 6th cohort (ENB-003 dose 2000ug). The dosing frequency for cohort 6 was doubled to 6 doses every 3 weeks from 6 doses every 6 weeks in cohort 1-5. The DCR across all cohorts irrespective of ETBR status was 33% (1 PR, 9 SD, 20 PD). The DCR in ETBR-Hi patients was 33% in cohorts 1-5 (4 SD, 1 PR, 10 PD) and 83% in cohort 6 (5 SD, 1 PD). The DCR for ETBR-Lo patients in cohort 6 was 0% (9 PD). ETBR-Lo patients were not enrolled in cohorts 1-5. For microsatellite stable (MSS) platinum

refractory/ resistant ovarian cancer there was an 80% DCR across all cohorts (1 PR, 3 SD, 1 PD) with a trend for durable responses at higher doses of ENB-003. A platinum refractory MSS ovarian cancer patient experienced a 95% PR of 12-month duration. The sample size was not powered for statistical significance.

“The completion of enrollment of the Phase 1 ENBOLDEN-101 first-in-man study is a significant milestone for our Company. We are extremely encouraged by the results in heavily treated cancer patients refractory to standard of care treatment,” stated Sumayah Jamal, MD-PhD, President, Chief Scientific Officer and Co-Founder of ENB Therapeutics. “Our data suggest potential efficacy in patients that do not historically respond to immunotherapy and support further clinical development. We are grateful to our patients and their families for their participation in our study. “

Part 2 is a dose expansion study at the recommended dose designed to evaluate the safety, tolerability and efficacy of ENB-003 in combination with pembrolizumab in cancers refractory to standard of care including MSS R/R ovarian cancer, MSS pancreatic cancer, anti-PD1 refractory HNSCC, anti-PD1 refractory melanoma and anti-PD1 refractory TNBC. For more information on this Phase 1/2a study, see NCT04205227.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

About ENB-003

ENB-003 is a selective endothelin B receptor (ETBR) inhibitor that, in preclinical studies, enhances efficacy of CAR-T and anti-PD-1 in solid tumors across multiple cancer types in preclinical studies. In an ongoing multi-center Phase 1/2 clinical trial, early efficacy signals suggest that ENB-003 overcomes resistance to the anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in heavily pre-treated drug resistant cancer patients. The Phase 2 portion of the ENB-003 + pembrolizumab combination study is expected to start in the first half of 2024. The trial will enroll microsatellite stable platinum refractory and primary platinum resistant ovarian cancer patients, as well as microsatellite stable pancreatic cancer patients that have failed standard of care.

About ENB Therapeutics, Inc.

ENB Therapeutics is a clinical-stage biopharmaceutical company developing a novel class of medicines, endothelin B receptor (ETBR) inhibitors, to overcome resistance to CAR-T in solid tumors and immune-based therapies such as the immune checkpoint inhibitors. ETBR causes uncontrolled cancer growth, drives cancers to spread through the body and prevents the immune system from detecting and killing cancer cells. ENB’s lead product candidate, ENB-003 specifically blocks the ETBR and has the potential to drive the efficacy of CAR-T and anti-PD1 therapies in solid tumors. ENB-003 is currently being investigated in an ongoing Phase 1/2 clinical trial in collaboration with Merck.

Learn more by visiting the ENB Therapeutics website.

Forward Looking Statements

This press release may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will” and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding the clinical development of ENB-003 or any of ENB’s other product candidates or programs; the design of ENB’s clinical trials; the safety, durability, or efficacy of ENB-003; and the potential benefits of ENB-003 or any of ENB’s other product candidates. ENB may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of ENB’s product candidates; availability and timing of results from preclinical studies and clinical trials; whether initial or interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the risk that trials and studies may be delayed and may not have satisfactory outcomes; expectations for regulatory approvals to conduct trials or to market product; risks to site initiation,

clinical trial commencement, patient enrollment and follow-up, as well as to ENB's abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements. Any forward-looking statements contained in this press release speak only as of the date hereof, and ENB expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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