SAFETY, EFFICACY, AND PHARMACOKINETIC RESULTS FROM A PHASE I FIRST-IN-HUMAN STUDY OF ABBV-151 WITH OR WITHOUT ANTI-PD1 MAB (BUDIGALIMAB) IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC SOLID TUMORS

Anthony Tolcher*, Desamparados Roda-Perez, Kai He, Victor Moreno, Carlos Gomez-Roca, Je-Pascal Madheli, Abituni Razak, Mohammad Saittou, Xiaowen Guan, Stany Jany-Daly, Rachel Leibman, Martha Blaney, James O’Brien, Patricia Lorusso, John Powely, Talia Golan, Kathy Miller, Jordi Bruix, NEXT Oncology, San Antonio, TX, USA; The Institute of Cancer Research, London, UK; The James Cancer Hospital, Columbus, OH, USA; START Madrid-FJD, Madrid, Spain; Institut Claudius Regaud/IUCT Oncopole, Marseille, France; Institut Roi Albert II Cancer Centre, Brussels, Belgium; Princess Margaret Cancer Center, Toronto, Canada; AbbVie, Inc., North Chicago, IL, USA; Yale Cancer Center, Yale University, New Haven, CT, USA; Carolina Biooncology Institute, Huntersville, NC, USA; Sheba Medical Center, Tel-Hashomer, Israel; Indiana University School of Medicine, Indianapolis, IN, USA; Hospital Clinic Barcelona, Barcelona, Spain

Background Glycoprotein-A repetitions predominant (GARP) is expressed on regulatory T-cells and modulates release of active transforming growth factor β1 (TGFβ1), an immunosuppressive cytokine. ABBV-151 is a first-in-class monoclonal antibody (mAb) that binds to the GARP-TGFβ1 complex, blocking the release of active TGFβ1. Preclinical data demonstrate that blocking GARP-TGFβ1 and programmed cell death protein-1 (PD-1) improves antitumor efficacy compared with anti-PD-1 alone. Combining ABBV-151 with the anti-PD-1 mAb budigalimab may enable increased antitumor efficacy by reducing the immunosuppressive effects of TGFβ1. Herein, we report preliminary safety, efficacy, and pharmacokinetic (PK) results from a first-in-human, phase 1 study (NCT03821935) assessing ABBV-151 ± budigalimab in adult patients (≥18 years) with locally advanced/metastatic solid tumors. Results from the all-comer dose escalation (ESC) phase and two cohorts from the dose expansion (EXP) phase are available: anti-PD-1/PD-ligand-1 naïve hepatocellular carcinoma (HCC) and anti-PD-1/PD-L1 relapsed/refractory urothelial cancer (UC).

Methods ESC patients must be refractory/intolerant to existing effective therapies; EXP cohorts have tumor-specific eligibility requirements. The primary ESC endpoint is the recommended phase II dose of ABBV-151 ± budigalimab. The primary EXP endpoint is preliminary efficacy of ABBV-151 + budigalimab, assessed by objective response rate per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Results As of June 2022, 157 patients have been enrolled, 57 in ESC (23 ABBV-151 monotherapy; 34 combination therapy) and 100 in EXP (including 36 UC; 12 HCC). As of January 2022, safety data were available for 129 patients. Any-grade adverse events (AEs) were reported in 119/129 (92%) patients. Most commonly: fatigue (28%), pruritus (27%), and nausea (22%). Grade 3-4 AEs occurred in 66/129 (51%) patients, with drug-related grade 3-4 AEs in 18/129 (14%) patients. ABBV-151 showed dose proportional PK. No antitumor responses were reported for the ABBV-151 monotherapy ESC cohorts. In the combination ESC cohorts, there were 4 confirmed responses, 1 unconfirmed response, and 4 patients had stable disease (SD) ≥6 months. In the anti-PD-1/PD-L1 relapsed/refractory UC EXP cohort, there were 5 confirmed responses, 1 unconfirmed response, and 5 patients had a best response of SD. In the anti-PD-1/PD-L1 naïve HCC EXP cohort, there were 5 confirmed responses, including one response per immune RECIST, and 3 patients had a best response of SD.

Conclusions ABBV-151 ± budigalimab showed a manageable safety profile in patients with advanced solid tumors. Preliminary efficacy results demonstrate durable antitumor activity with ABBV-151 + budigalimab, including in anti-PD-1 naïve HCC.

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Ethics Approval The study was approved by the Advarra Ethics Board, under the license number IRB00000971.