Phase 1 Safety Of ICOS Agonist Antibody JTX-2011 Alone and with Nivolumab (Nivo) in Advanced Solid Tumors; Predicted vs. Observed Pharmacokinetics (PK) in ICONIC

Howard A. Bunn III1, Margaret K. Caballero1, Anthony W. Tischler2, Shreya Kumar1, Gerald Steven Pachmayr3, Russell Kent Pachmayr1, Scott S. Tesh1, Geoffrey Thomas Garey3, Tanya Y. Sekwati4, Judith F. Ganem5, Patricia LoRusso5, Jonathan H. Ipp6, Fei Hu2, Manny Lazaro2, Myles Clancy1, Bayu Ding1, Elizabeth G. Huynh7, Timothy Anthony Yan9, Shivaani Kummar8, Scott V. Godfrey8, Jason S. Chen1. 1Bristol Myers Squibb, Nashville, TN; 2Memorial Sloan Kettering Cancer Center, New York, NY; 3MEMO San Antonio, TX; 4Georgia Institute of Technology, Atlanta, GA; 5Japan Cancer Research Institute at HealthONE, Denver, CO; 6Washington University School of Medicine in St. Louis, SA, MD; 7University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA; 8Georgia Lumbard Comprehensive Cancer Center, University of Chicago, IL; 9Massachusetts General Hospital, Boston, MA; 10Yale Cancer Center, New Haven, CT; 11Applied Biosystems, Lincoln, MA; 12Juniper Therapeutics, Cambridge, MA; 13MD Anderson Cancer Center, Houston, TX.

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Practical Pharmacology and Modeling

JTX-2011 is a humanized mAb against mononuclear CD28-related protein (CD28r) expressed on effector T-cells (CD28r). ICOS agonist in preclinical mouse syngeneic tumor models both as a single agent and in combination with PD-1 inhibitors.

- Single agent efficacy correlates with percentage of ICOS expressing immune cells in murine tumors
- There was similar is peripheral and intratumoral T cells in murine syngeneic tumor models
- Quantitative Systems Pharmacology (QSP) Modeling informed first-in-human dose selection based on:
  - Tumor and IgG1 PK data
  - In vivo and ex vivo data from mice (mAb and human IgG1 antibody)
- Preliminary for human PK and ICOS antibody (target engagement)
- First in human starting dose anticipated to have tiered ICOS target engagement (5µg/kg).

Table 1: Disposition as of May 12, 2017

Safety Results: JTX-2011 was dosed to the highest planned level (1 mg/kg for JTX-2011 as a single agent and 0.3 mg/kg for JTX-2011 + Nivolumab). In combination with Nivolumab, JTX-2011 demonstrated single agent activity.

- 5 patients developed a new adverse event that was not reported in combination with placebo
- 6 patients reported dose-limiting toxicities
- 2 DLTs (out of 6 subjects) occurred at 1 mg/kg JTX-2011

Table 2: Distribution of Toxicity Events

Table 3: Summary of JTX-2011 PK Parameters for All Solid Tumors (≤ 0.01mg/kg JTX-2011) and Combination with Nivolumab

Table 4: Summary of JTX-2011 PK Parameters for JTX-2011 + Nivolumab

Table 5: Summary of Most Frequent Related Adverse Events (≥25% in any column)

Table 6: Summary of Most Frequent Related Adverse Events (≥25% in any column)

Table 7: Summary of Most Frequent Related Adverse Events (≥25% in any column)

Table 8: Summary of Most Frequent Related Adverse Events (≥25% in any column)

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