**TITLE:** TAK-676: A Novel Stimulator of Interferon Genes (STING) Agonist Promoting Durable Interferon-Dependent Anti-Tumor Immunity in Preclinical Studies

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**Authors’ Disclosures**

YS, ECC, DM, VAA, SI, VK, AM, JS, MM, MY, JH, LS, SH, VS, CG, ERR, HB, SM, TT, PS, JC, AOA-Y, CWA, MHS, MO disclose employment with Takeda. OG discloses previous employment with Takeda and current employment with Invicro, LLC. TDT discloses previous employment with Takeda and current employment with Atara Biotherapeutics, Inc.

**SUPPLEMENTAL FIGURES**

**Supplementary Figure 1.** Cell viability of **A,** human monocyte derived dendritic cells by TAK-676 at 24 hours from 5 donors, and **B,** of mouse bone marrow derived dendritic cells up to 72 hoursfrom 2 donors.



**Supplementary Figure 2.** Mean plasma (left) and tumor (right) concentration–time curves of TAK-676 in BALB/c mice bearing A20 tumors after intravenous administration of TAK-676at 0.025, 0.125, 0.25, 0.5, and 2 mg/kg.



**Supplementary Figure 3.** Mean percent body weight change over time in: **A,** BALB/c mice bearing CT26.WT syngeneic tumors; **B,** BALB/c mice bearing A20 syngeneic tumors; All data shown are representative of at least three independent experiments.



**Supplementary Figure 4.** Mean percent body weight change over time in WT or STING-deficient C57BL/6J-Tmem173gt/J (Goldenticket) mice bearing STING WT or deficient B16-F10 syngeneic tumors dosed with vehicle or TAK-676.



**Supplementary Figure 5**. Cytokine responses in plasma (left) and tumor (right) in A20 tumor-bearing mice following exposure to a single intravenous dose of vehicle or TAK-676: **A**, TNF-α; **B**, MCP-1; and **C**, IL-6. All data shown are representative of at least three independent experiments.

Δ: Indicates that some samples in this group had values below the lower limit of quantitation of the assay or had values extrapolated beyond the standard range.

**\***: p value ≤ 0.05 relative to vehicle control.

\*\*: p value ≤ 0.01 relative to vehicle control.

\*\*\*: p value < 0.000001 relative to vehicle control.