ASP8374/PTZ 201
NON-CONFIDENTIAL SUMMARY
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## ASP 8374/PTZ 201 SUMMARY

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<tr>
<th>Project Code</th>
<th>A8374/PTZ201</th>
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<tr>
<td>Project Name</td>
<td>ASP8374/PTZ201</td>
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<tr>
<td>Mechanism of Action</td>
<td>Blocking binding of TIGIT ¹) to its ligands PVR ²) (CD155) and PVRL2 ³) (CD112) which functions as immune checkpoint</td>
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<td>Target Indication(s)</td>
<td>Solid tumors and potential hematologic malignancies</td>
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<td>Dosing and Administration</td>
<td>700mg/3weeks, iv infusion, until PD</td>
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<td>Latest Phase Development</td>
<td>P1</td>
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¹) TIGIT: T Cell Immunoreceptor With Ig And ITIM Domains  
²) PVR: PVR cell adhesion molecule  
³) PVRL2: Poliovirus receptor-related 2  
⁴) PD-1: Programmed cell death 1
TIGIT AS A TARGET

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a well validated immune checkpoint expressed on memory CD4+ & CD8+ T cells, Tregs, and NK cells.

- CD226/TIGIT is an immune checkpoint analogous to CD28/CTLA-4
  - CD226 provides a costimulatory signal to T cells
  - TIGIT provides a coinhibitory signal to T cells

- TIGIT ligands CD155 (PVR) and CD112 (PVRL2) are overexpressed in tumors, providing an immune suppressive environment.

- Anti-TIGIT blocking antibodies
  - Enhance T cell proliferation and IFN-γ secretion
  - Increase cytotoxic activity of NK cells

Competitors

- Roche/Genentech (Johnston RJ. Cancer Cell 2014);
  - FIH started in May 2016

- BMS (Chauvin J-M. JCI 2015)
TIGIT AS A TARGET

- TIGIT inhibition increases immune cell activity
- TIGIT is co-expressed with PD-1 in tumor infiltrating lymphocytes
  - Co-blockade of PD-1 and TIGIT ↑ proliferation & cytokine production in NY-ESO-1 specific CD8+ T cells

Inhibition of TIGIT on human T cells

Yu et al., Nat Imm 2009 10:48

Chauvin et al., JCI 2015

BMS antibody: Published Data
TIGIT AS A TARGET

- Combination of anti-PD1 and anti-TIGIT Abs demonstrated superior efficacy in tumor models

CT26 syngeneic mouse models were treated with isotype control (black), anti-PD-L1 + control (red), anti-TIGIT + control (blue), or anti-PD-L1 + anti-TIGIT (purple) antibodies for 3 weeks.
- Minimal activity observed with single agent anti-TIGIT or anti-PD-L1.
- Combination of anti-PD-L1 and anti-TIGIT demonstrated potent anti-tumor activity.

Johnson et al., Cancer Cell, 2014
Characterization of ASP8374, a fully-human, antagonistic anti-TIGIT monoclonal antibody

- ASP8374 stimulated cytokine production in cultured human primary cells
- ASP8374 in combination with pembrolizumab induced higher T-cell activation in vitro than either treatment alone
- An anti-mouse TIGIT antibody surrogate of ASP8374 elicited anti-tumor activity as monotherapy or in combination with anti-PD1 in syngeneic tumor models
- See reference and link below for full details

ASP8374/PTZ-201: HISTORY/STATUS

- MOA: Fully humanized IgG4 anti-TIGIT mAb that blocks binding of TIGIT to its ligands PVR and PVRL2
- Target Indications: Solid Tumors
- Pre-IND Meeting Request: Submitted to FDA on 13Jul2016
- IND Submission in 1Q2017
- Phase I – FSI 3Q2017
CLINICAL STUDIES THUS FAR

**ASP8374-CL-0101: Active study, Not enrolling**
A Phase 1b Study of ASP8374, an Immune Checkpoint Inhibitor, as a Single Agent and in Combination With Pembrolizumab in Subjects With Advanced Solid Tumors

**8374-CL-0102: Completed**
A Phase 1, Open Label Study of ASP8374, an Immune Checkpoint Inhibitor, in Japanese Patients with Advanced Solid Tumors

**IIT: Active, Not enrolling yet.**
Phase Ib Trial of ASP8374 and Cemiplimab in Recurrent Malignant Glioma Patients.
INTELLECTUAL PROPERTY

Patents covering ASP8374

• **Substance Patent Family: WO/2017/059095 (filed on Sep. 29, 2016)**
  - **Granted**: Indonesia, Russia, South Africa, US
  - **Pending**: Argentina, Australia, Brazil, Canada, China, Colombia, Europe, Gulf Coast, Hong Kong, Israel, India, Indonesia, Japan, Malaysia, Mexico, Philippines, Russia, Singapore, South Africa, South Korea, Thailand, Taiwan, Ukraine, US, Vietnam

  - **Pending**: Australia, Brazil, Canada, China, Colombia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Jordan, Malaysia, Mexico, Philippines, Russia, Singapore, South Africa, South Korea, Thailand, Ukraine, US, Vietnam