**FDA/HESI-ITC Workshop on Preclinical and Translational Safety Assessment of CD3 Bispecifics**

The mission of HESI, is to collaboratively identify and help to resolve global health and environmental challenges. The Immunotoxicology Technical Committee (ITC) is one of the HESI Scientific Technical Committees and is composed of Scientists from Industry, Academia and Government (http://hesiglobal.org/immunotoxicology/). The HESI-ITC identifies and addresses scientific issues related to the development and application of immunotoxicology to public health and human health risk assessment; promotes the understanding and appropriate use of immunotoxicologic data to protect human health; and contributes substantively to the scientific decision-making processes relative to the development of guidelines and regulations for immunotoxicologic testing at the local, national, and international levels.

**Workshop Dates and Location: 1st - 2nd October, 2018 at US FDA Silver Spring, MD**

**Goal:** The goal of this workshop is to discuss the preclinical and translational safety assessment of CD3 bispecific therapies, focusing on 8 topics as described based on sessions below.  The intent is to have multiple short talks (~10-20 min each) followed by longer in-depth discussion within each session.  To this end, we are actively recruiting speakers and attendees from Institutions working actively in the area of CD3 bispecifics or areas with overlapping safety concerns.

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| **Day 1, Monday, October 1, 2018** | **Topic** |
| **8:00 AM – 8:15 AM** | **Welcome and Opening remarks – Jacintha Shenton** |
| **8:15 AM – 9:00 AM** | **Keynote: Blincyto® The First Approved BiTE® Antibody Construct**Speaker: * Benno Rattel, Amgen

Discussion |
| **9:00 AM – 9:30 AM** | **Session 1.  CD3 bispecifics and their effect on T cell biology** **(Moderator: Cris Kamperschroer, Pfizer)**Hallmarks of activitySpeaker: * *CD3 bispecifics and their effect on T cell Biology: Hallmarks of Activity*  - Jessica Kirshner, Regeneron

Discussion |
| **9:30 AM – 10:50 AM (15 min break)** | **Session 2. Target (tumor antigen) expression and liability assessment** **(Moderators: Hervé Lebrec, Amgen and Rafael Ponce, Juno Therapeutics)**Speakers:* *Title pending* (Target liability assessment tools and case studies) - Herve Lebrec, Amgen
* *Title pending* - Oliver Thomas, Amgen
* *Title pending* (Consequences of misleading publicly available target sequence info and underestimation of risk prior to toxicology study conduct) - Liz Bogaert, Xencor

Discussion |
| **10:50 AM – 12:30 PM**  | **Session 3.**  **Impact of construct design and CD3 and/or tumor antigen binding affinity on bioactivity, safety and efficacy (Moderators: Jacintha Shenton, Janssen and Paul Moore, MacroGenics)** Speakers:* Introduction to Various Constructs in Use Adam Root, Pfizer
	+ *Title pending* - Ezio Bonvini, MacroGenics
	+ *Title pending* - Jennifer Richardson, Cytomyx
	+ *Affinity tuning of targeting Fabs for T-cell dependent bispecific molecules* - Karin Staflin, Genentech
	+ *On-target toxicity of a CD3 bispecific: can variation in affinity lead to different outcome in preclinical studies*? - Anna Maria Giusti, Roche

Discussion |
| **12:30 PM – 1:15 PM** | **Lunch** |
| **1:15 PM – 4:35 PM (15 min break)** | **Session 4.  In vivo pharmacology and toxicology** **(Moderators: Oliver Thomas, Amgen and Gautham Rao, Genentech)**Speakers: * *Title pending* - Charles Sentman, Dartmouth
* *Testing efficacy and safety of bispecific antibodies in mouse models*  - Jessica Kirshner, Regeneron
* *Title pending* - Rachel Beaulieu Goldsmith, Janssen
* *Title pending* - Shoba Shetty, Janssen
* *Blocking Cytokines Induced by CD3 Bispecifics and Impacts on T Cell Responses*  - Cris Kamperschroer, Pfizer
* *Title pending* Amy Sharma, Genentech
* *Title pending* - Chidozie Amuzie, Janssen
* *Preclincial evaluation of TCR bispecifics targeting cancer-specific HLA ligands in the absence of relevant animal models* - Frank Schwobel, Immatics
* *A nonclinical approach for predicting clinical safety with novel, human-specific, TCR-based CD3 bispecific ImmTAC molecules. -* Joseph Dukes, Immunocore
* *Safety strategy applied to p-MHC TCR-like CD3 bispecific antibodies in the absence of cross-reactive animal species -*  Estelle Marrer-Berger, Roche
* *Title pending* - Ajai Pal, Glenmark

Discussion |

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| **Day 2, Tuesday, October 2, 2018** |
| **8:00 AM – 9:15 AM** | **Session 5. In vitro assays to assess cytokine release** **(Moderators: Cris Kamperschoer, Pfizer and Jacintha Shenton, Janssen)**Speakers:* *Target Biology and CRA Assay Format* - Dan Weinstock, Janssen
* *In vitro assessment of BiTE-induced cytokine release* - Matthias Friedrich, Amgen

Discussion |
| **9:15 AM – 9:30 AM** | **BREAK**  |
| **9:30 AM – 11:30 AM**  | **Session 6.  FIH dose selection** **(Moderators: John Leighton, US FDA and Dan Rock, Amgen)**Speakers:* *Title pending* - Alison Betts, Pfizer
* *An FDA analysis of CD3 bispecifics and approaches to first-in-human dose selection* - Tiffany Ricks, US FDA
* *Title pending* - Dan Rock, Amgen

Discussion |
| **11:30 AM – 12:15 PM** | **LUNCH** |
| **12:15 PM – 2:00 PM** | **Session 7. Clinical experience** **(Moderators: Yvette Kasamon, US FDA and Paul Moore, Macrogenics)**Speakers:* *Title pending* - Dirk Nagorsen, Amgen
* *Title pending* -Jenna Goldberg, Janssen
* *Title pending* - Najat Bouchkouj, US FDA
* *Title pending* - Tae Han, Amphivena Therapeutics

Discussion |
| **2:00 PM – 2:15 PM** | **BREAK** |
| **2:15 PM – 3:45 PM** | **Session 8. Translation of nonclinical findings to the clinic** **(Moderators: Oliver Thomas, Amgen and Hervé Lebrec, Amgen)**Speakers: * *Title pending* - Weirong Wang, Janssen
* *Title pending* - Paul Moore, Macrogenics

Discussion |
| **3:45 PM – 4:15 PM** | **Final thoughts/ Discussion** |