
Supplementary information

Targeted protein degraders: a call for collective action to advance safety assessment

In the format provided by the authors

I. Event details

Full details of the workshop are available in the public event page on HESI's website at: hesiglobal.org/event/hesi-protacs-and-molecular-glues-safety-workshop

Workshop Planning Committee Organizations: AbbVie, Almirall, Amgen, Apconix, Bayer AG, Bristol Myers Squibb, C4 Therapeutics, Dana Farber Cancer Institute, Kymera Therapeutics, Novartis, Pfizer Inc., Roche, Sanofi, Stanford University, Merck & Co., Inc, Janssen Pharmaceuticals, HESI, Synergy Medicines, UCB, US FDA, UK MHRA

Workshop Coordinators: Connie Mitchell (HESI Scientific Program Manager); Cyril Pettit (HESI Executive Director).

II. Agenda

Thursday October 14, 2021	Topic
10:00-10:15	Welcome and Opening Remarks: Dr. Ruth Roberts, ApconiX, and Dr. Cyril Pettit, HESI
10:15-11:00	Background and Biology: definitions, scope, de-risking molecules versus de-risking targets Speaker: Dr. Lyn Jones, Dana Farber Cancer Institute
11:00-12:30	Screening and Applied De-Risking Strategies Rapporteur: Dr. Mira Pavkovic, Bayer <u>Case Studies</u> 11:00-11:10 Leveraging pharmacology experiments for safety data – Dr. Mira Pavkovic, Bayer 11:10-11:20 <i>Discussion/Q&A</i> 11:25-11:35 A Proteomic Platform to ID Off-Target Proteins Associated with Therapeutic 11:35-11:50 Modalities that Induce Protein Degradation/ Gene Silencing – Dr. Fan Fan, Amgen, <i>Discussion/Q&A</i> 11:50-12:05 Teratogenic Effects of IMiDs across species and discovery of SALL4 as a target – Dr. Katie Stamp, BMS 12:05-12:15 <i>Discussion/Q&A</i> 12:15-12:30 Session Discussion and Summary
12:30-12:40	Break
12:40-15:30	Assessment of ADME, Solubility, PD, and other Considerations Rapporteur: Dr. Laurie Volak, Janssen <u>Case Studies:</u> 12:40-12:55 Tissue distribution of PROTACs in mice – Dr. Andreas Reichel & Dr. David Banczyk, Bayer 12:55 -13:10 <i>Discussion/Q&A</i> 13:10-13:25 DMPK optimization challenges for degraders – Dr. Matthias Wittwer & Dr. Carina Cantrill, Roche 13:25-13:40 <i>Discussion/Q&A</i> 13:40-13:55 Insights into ADME Issues for PROTACs – Dr. Matthew Hoffman, BMS, 13:55-14:10 <i>Discussion/Q&A</i> 14:10-14:20 Break 14:20-14:35 ADME Methods to Overcome Technical Challenges in the in vitro Assays for TPD Molecules – Dr. Dapeng Chen, Kymera 14:35-14:50 <i>Discussion/Q&A</i> 14:50-15:05 Importance of accurate protein binding measurements for establishing PK/PD in vitro-in vivo 15:05-15:20 correlation (IVIVC) – Dr. Laurie Volak & Dr. Meghan Pryor, Janssen, <i>Discussion/Q&A</i> 15:20-15:30 <i>Session Discussion and Summary</i>
15:30	Adjourn Day 1

Friday October 15, 2021	Topic
10:00-10:10	Welcome and Day 1 Recap Ms. Connie Mitchell, HESI
10:10-12:00	Role of Different e3 ligases Rapporteur: Dr. James Sidaway, ApconiX Case Studies: 10:10-10:35 Role of different E3 ligases – a case study to exploit tissue selective E3 ligases - Dr. Hakryul Jo, Kymera 10:35-10:50 <i>Discussion/Q&A</i> 10:50-11:05 E3 ligases and PNS effects – Dr. Natasa Zamurovic, Novartis 11:05-11:20 <i>Discussion/Q&A</i> 11:20-11:35 In vivo tox comparison of dog vs NHP using cereblon mediated degrader – Dr. Michelle Hemkens, Pfizer 11:35-11:50 <i>Discussion/Q&A</i> 11:50-12:00 Combined Discussion and Summary
12:00-12:10	Break
12:10-14:00	Species Selection and Selectivity Rapporteur: Dr. Madeline Fort, Amgen Case Studies: 12:10-12:30 How to select a pharmacologically relevant species for cereblon modulators – Dr. Katie Stamp, BMS 12:30-12:45 <i>Discussion/Q&A</i> 12:45-13:00 In vitro shifts in potency across species – Dr. Andrew Burdick, Pfizer 13:00-13:15 <i>Discussion/Q&A</i> 13:15-13:30 Computational approaches in early safety assessment of protein degraders – Dr. Mohan Rao, Janssen 13:30-13:45 <i>Discussion/Q&A</i> 13:45 – 14:00 Combined Discussion and Summary
14:00-14:10	Break
14:10-14:40	Regulatory Science Panel Discussion and Key Summaries Moderator: • Dr. Jim MacDonald, Synergy Medicines Panel: • Dr. Ian Waterson, MHRA • Dr. Jeff Summers, FDA • Dr. Brad Enerson, Kymera
14:40-15:15	Final thoughts/ Discussion What does this evaluation of the null hypothesis tell us about how we can move forward as a community to advance safety and development? How do we best support critical patient populations safely and efficiently for PROTACs and Molecular Glues? Moderators: Dr. Ruth Roberts, ApconiX and Dr. Lise Loberg, AbbVie
15:15	Meeting Adjourn

III. List of participants

Registered participants

First Name	Last Name	Organization
Tinya	Abrams	Novartis
Norma	Alcaraz	Bristol Myers Squibb
Laura	Armstrong	Bristol Myers Squibb
Kumar	Ashtekar	Yale University
Amy	Aslamkhan	Merck & Co., Inc.
Christian	Atsriku	Schrodinger Inc
Josef	Auburger	Bayer AG
Karen	Augustine	Bristol Myers Squibb
Mariona	Auli	Almirall
David	Banczyk	Bayer AG
Alexandra	Barajas	Northwestern University
Kent	Barbay	Janssen Pharmaceuticals
Paul	Barrow	Roche
Raphaelle`	Berger	Merck & Co., Inc.
Didier	Berthelot	Janssen Pharmaceuticals
Peter	Beyrouthy	AbbVie
Ridhirama	Bhuwania	Bayer AG
Simone	Bonazzi	Novartis
Martin	Bopst	Roche
Christopher	Bowman	Pfizer
Katharine	Bray-French	Roche
JF	Brazeau	Janssen Pharmaceuticals
Alessandro	Brigo	Roche
Ruud	Bueters	Janssen Pharmaceuticals
Andrew	Burdick	Pfizer
Carina	Cantrill	Roche
Philip	Carpino	Janssen Pharmaceuticals
Kendal	Carrow	Northwestern University
Annie	Caudle	Janssen Pharmaceuticals
Annick	Cauvin	UCB
Charu	Chaudhry	Janssen Pharmaceuticals
Connie	Chen	HESI
Dapeng	Chen	Kymera Therapeutics
Yenwei	Chen	UCLA
An	Chi	Merck & Co., Inc.
Alessio	Ciulli	University of Dundee
Jon	Cook	Pfizer
Philippe	Couttet	Novartis
Philipp	Cromm	Bayer AG
Richard	D'Aquila	Northwestern University
Myrtle	Davis	Bristol Myers Squibb
Alberto	del Rio	Novartis
Anthony	DeLise	Novartis
Rex	Denton	Bristol Myers Squibb
Patrick	Devine	Novartis
Keith	Di Petrillo	Bristol Myers Squibb
Gabriele	Dietert	Sanofi
Karen	Dingley	Schrodinger Inc
John	Dougherty	US FDA
Yvonne	Dragan	Takeda
Sara	Dunne	Northwestern University
Heidrun	Ellinger-Ziegelbauer	Bayer AG
Brad	Enerson	Kymera Therapeutics

Therese	Eriksson Faelker	Bayer AG
Patricia	Escobar	Merck & Co., Inc.
Raymond	Evers	Janssen Pharmaceuticals
Fan	Fan	Amgen Inc.
Yunlan	Fang	Bristol Myers Squibb
Mozhgan	Farshbaf	Amgen Inc.
Mara	Fattah	Northwestern University
Joel	Federspiel	Pfizer
Lijin	Feng	Amgen Inc.
Mireia	Fernandez Ocana	Pfizer
Elise	Forst	Northwestern University
Madeline	Fort	Amgen Inc.
Matthias	Friedrich	Amgen Inc.
Mirjam	Fröhlicher	Novartis
Angela	Garau	Italian Medicines Agency
Suzanne	Gaudet	Novartis
Anja	Giese	Bayer AG
Patricio	Godoy	Roche
Raymond	Gonzalez	Merck & Co., Inc.
Andrew	Goodwin	US FDA
Nathanael	Gray	Stanford University
Niels	Griesang	Sanofi
Vitalina	Gryshkova	UCB
Gary	Gu	Novartis
Magali	Guffroy	AbbVie
Roberto	Guzman	Bristol Myers Squibb
Kemal	Haque	Apconix
Nicholas	Hastings	Merck & Co., Inc.
Michelle	Hemkens	Pfizer
Geraldine	Hernandez	Bristol Myers Squibb
Herbert	Himmel	Bayer AG
Brad	Hirakawa	Pfizer
Matthew	Hoffmann	Bristol Myers Squibb
Andreas	Hofmann	Novartis
Andreas	Hohlbaum	Sanofi
Kristen	Holbrook	Amgen Inc.
Michelle	Horner	Amgen Inc.
Meng-Yang	Hsiao	Janssen Pharmaceuticals
Katie	Hsu	Amgen Inc.
Hui	Huang	Janssen Pharmaceuticals
Corina	Hunger	Sanofi
Elisabeth	Husr	Roche
Daher	Ibrahim Aibo	Novartis
Frank	Jacobs	Janssen Pharmaceuticals
Brandon	Jeffy	Takeda
Hakryul	Jo	Kymera Therapeutics
Benjamin	Johnson	Bristol Myers Squibb
Lyn	Jones	Dana Farber Cancer Institute
David	Jones	UK MHRA
Beth	Joshi	Bristol Myers Squibb
Marlene	Juedes	Roche
Vijaykumar	Kale	Amgen Inc.
Soumya	Kandi	Northwestern university
Sule	Karaman	Novartis
Michael	Kiffe	Novartis
Jacqueline	Kinyamu-Akunda	Janssen Pharmaceuticals
Richard	Knight	Apconix
Victoria	Koch	Roche
Rebecca	Kohnken	Abbvie

Johannes	Kopf	Bayer AG
Katja	Kotlenga	Sanofi
David	La	Janssen Pharmaceuticals
Tejas	Lahoti	Takeda
Joan	Lane	Amgen Inc.
Yanbin	Lao	Bristol Myers Squibb
John	Lapek	Pfizer
Fabrice	LeBoeuf	Health Canada
Ling	Liu	Pfizer
Lise	Loberg	AbbVie
Danielle	Loskot	Janssen Pharmaceuticals
Kaitlyn	Lovato	Janssen Pharmaceuticals
Laura	Luh	Bayer AG
Brian	Ly	Janssen Pharmaceuticals
Jim	MacDonald	Synergy Medicines
Alexander	Marker	Sanofi
Lisa	Marroquin	Pfizer
Donald	Marsh	Merck & Co., Inc.
Mike	Mendelsohn	US EPA
Sheroy	Minocherhomji	Amgen Inc.
Connie	Mitchell	HESI
Sonia	Miranda	Novartis
Ashley	Modell	Broad Institute of MIT and Harvard
Susanne	Mohr	Roche
Basudeb	Mondal	Broad Institute of MIT and Harvard
Silvia	Moore	Bristol Myers Squibb
Lucilia	Mouries	HESI
Minh	Nguyen	Janssen Pharmaceuticals
Daniel	Oehrich	Janssen Pharmaceuticals
Nobumichi	Ohoka	National Institute of Health Sciences (Japan)
Tim	Pastoor	Oearth Bio
Nirav	Patel	Sanofi
Katherin	Patsch	University of Southern California
Mira	Pavkovic	Bayer AG
Richard	Peterson II	AbbVie
Syrl	Pettit	HESI
Colin	Phipps	AbbVie
Joseph	Piccotti	Schrodinger Inc
Karen	Price	Bristol Myers Squibb
Meghan	Pryor	Janssen Pharmaceuticals
Ruomeng	Qiu	Northwestern University
Yusheng	Qu	Amgen Inc.
Radha	Ramakrishnan	Bristol Myers Squibb
Mohan	Rao	Janssen Pharmaceuticals
Benno	Rattel	Amgen Inc.
Andreas	Reichel	Roche
Carlis	Rejon	Health Canada
Alan	Reynolds	US EPA
Michael	Rheaume	Bristol Myers Squibb
Stephan	Riedmaier	Bristol Myers Squibb
Ruth	Roberts	Apconix
Miquel	Salva	Almirall
Jennifer	Sander	Bayer AG
Aubrey	Sawyer	Northwestern University
Georg	Schmitt	Roche
Anneliese	Schneider	Roche
Martin	Schneider	Novartis
Carolyn	Schramm	UCB
Maja	Sedic	Sanofi

Jason	Sello	University of California San Francisco
Mary	Shaw	Bayer AG
Wen	Shen	Pfizer
Roman	Shimanovich	Schrodinger Inc
Artem	Shkumatov	Amgen Inc.
Wen Chyi	Shyu	Takeda
James	Sidaway	Apconix
Phumzile	Sikakana	Apconix
Kurtis	Sims	Bristol Myers Squibb
Marijke	Somers	Janssen Pharmaceuticals
Chisu	Song	Northwestern University
Stan	Spence	C4 Therapeutics
Katie	Stamp	Bristol Myers Squibb
Claudia	Stark	Bayer AG
Rowan	Stringer	Novartis
Jeffrey	Summers	US FDA
Isaiah	Swauncy	Janssen Pharmaceuticals
Yuen	Tam	Janssen Pharmaceuticals
Matthew	Tang	Health Canada
Yang	Tang	Bristol Myers Squibb
Satbir	Thakur	Health Canada
Mark	Tichenor	Janssen Pharmaceuticals
Laszlo	Urban	Novartis
Cristina	Vaca	Northwestern University
Jean-Pierre	Valentin	UCB
Sreekanth	Vedagopuram	Broad Institute of MIT and Harvard
Jennifer	Venabl	Janssen Pharmaceuticals
Hariharan	Venkatesan	Janssen Pharmaceuticals
Axel	Vicart	Novartis
Laurie	Volak	Janssen Pharmaceuticals
Xiaoting	Wang	Amgen Inc.
Max	Wang	Northwestern University
Shaomeng	Wang	University of Michigan
Ronald	Wange	US FDA
Kerstin	Wäse	Sanofi
Ian	Waterson	MHRA
Teresa	Wegesser	Amgen Inc.
Henry	Weiss	Northwestern University
Kara	Welch	US EPA
Matthias	Wittwer	Roche
Amy	Yang	Pfizer
Gina	Yanochko-Hoffman	Janssen Pharmaceuticals
Tomoya	Yukawa	Takeda
Natasa	Zamurovic	Novartis
Xiaoyu	Zhang	Northwestern University
Guangron	Zheng	University of Florida
Verena	Ziegler	Bayer AG