PRAME Phase 1 study of brenetafusp (IMC-F106C) in cutaneous melanoma

May 31, 2024
Forward Looking Statements

This presentation contains “forward-looking statements” within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as “may”, “will”, “believe”, “expect”, “plan”, “anticipate” and similar expressions (as well as other words or expressions referencing future events or circumstances) are intended to identify forward-looking statements. All statements, other than statements of historical facts, included in this presentation are forward-looking statements. These statements include, but are not limited to, statements regarding Immunocore’s ImmTAC platform, including its ability to predict clinical benefit; statements regarding the expected clinical benefits of KIMMTRAK, brenetafusp (IMC-F106C) and Immunocore’s other product candidates, including overall response rate and progression free survival and extended overall survival benefit, tumor reduction, ctDNA molecular response and extended overall survival benefit, the expected safety, efficacy and tolerability of Immunocore’s products and product candidates, including brenetafusp and tebentafusp, alone and in combination with other therapies; and the Company’s expectations regarding the design, progress, timing, scope and results of Immunocore’s existing and planned clinical trials, including the Phase 1/2 dose escalation trial with brenetafusp in patients with multiple solid tumor cancers including non-small cell lung cancer, small-cell lung cancer, endometrial, ovarian, cutaneous melanoma, and breast cancers, the Phase 3 PRISM-MEL301 trial with brenetafusp plus nivolumab and the converted Phase 3 trial evaluating KIMMTRAK for previously treated advanced cutaneous melanoma. Any forward-looking statements are based on management’s current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual events or results to differ materially and adversely from those set forth in or implied by such forward-looking statements, many of which are beyond Immunocore’s control. These risks and uncertainties include, but are not limited to, that interim data, data from any interim analysis of ongoing clinical trials and data from completed clinical trials may not be predictive of future trial results, the impact of worsening macroeconomic conditions on Immunocore’s business, financial position, strategy and anticipated milestones, including Immunocore’s ability to conduct ongoing and planned clinical trials; Immunocore’s ability to obtain a clinical supply of current or future product candidates or commercial supply of KIMMTRAK or any future approved products, including as a result of health epidemics or pandemics, war in Ukraine, the conflict between Hamas and Israel, the broader risk of a regional conflict in the Middle East, or global geopolitical tension; Immunocore’s ability to obtain and maintain regulatory approval of its product candidates, including KIMMTRAK; Immunocore’s ability and plans in continuing to establish and expand a commercial infrastructure and to successfully launch, market and sell KIMMTRAK and any future approved products; Immunocore’s ability to successfully expand the approved indications for KIMMTRAK or obtain marketing approval for KIMMTRAK in additional geographies in the future; the delay of any current or planned clinical trials, whether due to patient enrollment delays or otherwise; Immunocore’s ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; competition with market opportunities; unexpected safety or efficacy data observed during preclinical studies or clinical trials; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials or future regulatory approval; Immunocore’s need for and ability to obtain additional funding, on favorable terms or at all, including as a result of worsening macroeconomic conditions, including changes inflation and interest rates and unfavorable general market conditions, and the impacts thereon of the war in Ukraine, the broader risk of a regional conflict in the Middle East, the conflict between Hamas and Israel, and global geopolitical tension; Immunocore’s ability to obtain, maintain and enforce intellectual property protection for KIMMTRAK or any product candidates it or its collaborators are developing; and the success of Immunocore’s current and future collaborations, partnerships or future regulatory approvals or licensing arrangements, including the risk that Immunocore may not realize the anticipated benefits of its collaboration with Bristol Myers Squibb. These and other risks and uncertainties are described in greater detail in the section titled “Risk Factors” in Immunocore’s filings with the Securities and Exchange Commission, including Immunocore’s most recent Annual Report on Form 10-K for the year ended December 31, 2023 filed with the Securities and Exchange Commission on February 28, 2024, as well as discussions of potential risks, uncertainties, and other important factors in Immunocore’s subsequent filings with the Securities and Exchange Commission.

All forward looking statements contained in this presentation speak only as of the date on which they were made and should not be relied upon as representing its views as of any subsequent date. Except to the extent required by law, Immunocore undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Certain information contained in this presentation relates to or is based on studies, publications, surveys, and other data obtained from third party sources and Immunocore’s own internal estimates and research. While Immunocore believes these third party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy, or completeness of, any information obtained from third party sources.

KIMMTRAK™ is a trademark owned or licensed to Immunocore.
Agenda

Welcome
Bahija Jallal, CEO

Insights from KIMMTRAK
David Berman, Head of R&D

Phase 1/2 study of brenetafusp targeting PRAME
Dr. Diwakar Davar, UPMC

Q&A Session
Pioneering a new class of immunotherapy
KIMMTRAK: OS and PFS benefit with unique mechanism of action

T cell infiltration into tumors

In pre-clinical studies...

→ Distinct mechanism of action than checkpoints

In tumor biopsies...

→ More robust T cell infiltration and activation than checkpoints

In Phase 1-3...

→ Measuring full clinical benefit different than checkpoints

1 Hamid O J Trans Med 2011; 9: 204; Higgs et al., Clin Can Res 2018; 24: 3857; Postel-Vinay, JITC 2023; 11:e005301. ImmTAC: immune mobilizing monoclonal TCR against cancer
Case Study: clinical benefit in patient with SD and tumor reduction (-7%) due to necrosis and inflammation

Cutaneous melanoma patient\textsuperscript{1} KIMMTRAK monotherapy Ph 1
Definition of KIMMTRAK benefit broader than RECIST ORR

24% patients (11% PR + 13% SD with confirmed tumor reduction)- durable with median 11 mo.

SD patients with tumor reduction have same durability as PR (both 11 months)

Similar observation in 2L+ mUM, ASCO 2024 poster #9529

Durability of response

SD with tumor reduction* 11 months median duration reduction

PR/CR 11 months median duration response

*Phase 3 KIMMTRAK Trial (IMCgp100-202); *Defined as: any tumor reduction that is confirmed during at least one subsequent scan without intervening progression.
Disease control rate, strong predictor of significant PFS

DCR mostly of stable disease (SD)

Disease control rate

KIMMTRAK

<table>
<thead>
<tr>
<th></th>
<th>SD</th>
<th>PR/CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>22%</td>
<td>5%</td>
</tr>
<tr>
<td>27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Both PR and SD very durable

Drives PFS benefit

PFS HR 0.73

OS (HR 0.51) best endpoint to capture all benefit

*Hassel JC, et al. NEJM 2023 (Phase 3 KIMMTRAK Trial (IMCgp100-202)); The duration of tumor reduction was based on principles of RECISTv1.1 duration of response (DoR)
KIMMTRAK activity higher in early lines of therapy vs 2L+

1L KIMMTRAK

N=128

Clearance

Molecular response

12% 7% 44% pts 37% pts

2L+ KIMMTRAK

N=94

Clearance

Molecular response

29% pts 19% 39% pts 13% pts

ctDNA reduction is early surrogate of OS benefit and independent of CT/MRI

T cell fitness in blood important parameter of ImmTAC benefit

T cell fitness defined by Naïve and T stem cell (T_{scm}) blood signature

More data this year

Similar association between T cell fitness and CAR-T and TILs

Insights from KIMMTRAK that can be applied to ImmTAC platform

→ **Distinct MoA with more robust T cell infiltration and activation than checkpoints**
  - Distinct measures of benefit required - broader than RECIST ORR

→ **Disease control, including durable tumor reduction, is a hallmark of platform**
  - High DCR provides confidence for PFS in Phase 3

→ **ImmTAC activity higher in early lines of therapy vs 2L+**
  - Endogenous T cell fitness in blood important parameter of activity
Diwakar Davar, MD, MS
Clinical Director of the Melanoma and Skin Cancer Program, University of Pittsburgh Medical Center (UPMC) Hillman

→ Board-certified in internal medicine and medical oncology and completed both his residency and fellowship at UPMC

→ Clinical interests include management of advanced melanoma and the development of early phase studies to test novel immunotherapeutic approaches individually and in combination in patients with advanced cancer

→ Oversees the melanoma and skin cancer clinical trials portfolio at UPMC
Phase 1 safety and efficacy of brenetafusp (IMC-F106C), a PRAME × CD3 ImmTAC bispecific, in post-checkpoint cutaneous melanoma (CM)

Omid Hamid¹, Anja Williams², Juanita Lopez³, Daniel Olson⁴, Takami Sato⁵, Heather Shaw⁶, Claire F. Friedman⁷, Fiona Thistlethwaite⁸, Mark R. Middleton⁹, Celeste Lebbe¹⁰, Vincent T. Ma¹¹, Benjamin Izar¹², Peter Lau¹³, Oliver Bechter¹⁴, Peter Kirk¹⁵, Yuan Yuan¹⁶, Shannon Marshall¹⁶, and Diwakar Davar¹⁷

¹The Angeles Clinical and Research Institute, a Cedars-Sinai Affiliate, Los Angeles, CA; ²Sarah Cannon Research Institute, London, United Kingdom; ³The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; ⁴University of Chicago, Comprehensive Cancer Center, Chicago, IL; ⁵Sidney Kimmel Cancer Center, Jefferson University, Philadelphia, PA; ⁶University College London Hospital, London, United Kingdom; ⁷Memorial Sloan Kettering Cancer Center, New York, NY; ⁸The Christie NHS Foundation and University of Manchester, Manchester, United Kingdom; ⁹Medical Sciences Division, University of Oxford, Headington, Oxford, United Kingdom; ¹⁰Université Paris Citée, Dermatolo-Oncology AP-HP Hôpital Saint-Louis, INSERM U976, Paris, France; ¹¹University of Wisconsin Carbone Cancer Center, Madison, WI; ¹²Columbia University Medical Center, New York, NY; ¹³Linear Clinical Research, Harry Perkins Institute for Medical Research, Nedlands, WA, Australia; ¹⁴UZ Gasthuisberg - Katholieke University Leuven, Leuven, Belgium; ¹⁵Immunocore, Abingdon, United Kingdom; ¹⁶Immunocore, Rockville, MD; ¹⁷University of Pittsburgh Medical Center, Hillman Cancer Center, Pittsburgh, PA
Disclosures

Consulting: ACM Bio, Ascendis, Castle, Clinical Care Options (CCO), Gerson Lehrman Group (GLG), Immunitas, Medical Learning Group (MLG), Replimmune, Trisalus, Xilio Therapeutics;

Contracted Research for Institution: Arcus, Immunocore, Merck, Regeneron Pharmaceuticals Inc., Tesaro/GSK;

Royalties: None.

Speaker: Castle Biosciences.

Stock: Zola

Disclaimer

All statements contained in this presentation are based on preclinical and clinical trial data related to an investigational molecule, IMC-F106C. Development of this molecule is ongoing and, therefore, statements relating to study data to date should not be regarded as definitive reflections of safety, efficacy or the risk-benefit profile of the molecule.
Brenetafusp: ImmTAC bispecific T cell engager targeting HLA-A2-presented peptide from PRAME

TCR bispecific ImmTAC molecules redirect polyclonal T cells to target cancer cells by recognizing intra-/extra-cellular cancer proteins

ImmTAC platform validated by tebentafusp (gp100 × CD3) with OS (HR 0.51) and PFS benefit (HR 0.73) in mUM

ImmTAC tolerability with immune checkpoints demonstrated with tebentafusp in cutaneous melanoma

PRAME is broadly expressed in several tumor types, including ~90% cutaneous melanoma (CM), with minimal normal tissue expression

ImmTAC, Immune mobilizing T cell receptor Against Cancer; mUM, metastatic uveal melanoma; OS, overall survival; TCR, T cell receptor

1. Internal IHC data analysis and TCGA; Kaczorowski, et al. 2022 Am J Surg Pathol 2022; 46(11):1467-1476
**Brenetafusp Phase 1/2 Study Design**

**Key objectives:**
- **Primary**
  - Safety
  - MTD/expansion dose
  - Efficacy (in expansion only)
- **Additional**
  - Pharmacokinetics
  - Molecular response (ctDNA)
  - Predictive biomarkers

**Key eligibility criteria for CM:**
- Unresectable or metastatic
- HLA-A*02:01 (central testing)
- Previously treated with
  - immune checkpoint inhibitors
  - BRAFi/MEKi, if applicable

**Dose escalation**
- RECIST tumor assessment every 9 weeks
- ctDNA assessment every 3 weeks

**Expansion**
- Cutaneous melanoma
- Ovarian
- NSCLC
- Endometrial

**Results from N=47***

**Weekly IV infusion**
- **1-2 step doses**
- **Target dose**

**Initial results from N=9**

**Results from N=47***

**Weekly IV infusion**
- **1-2 step doses**
- **Target dose**

**Chemotherapy combinations**
- Pembrolizumab combination
- Other combinations

**EudraCT No. 2019-004046-16; NCT04262466**
Data cut-off date: 18-Mar-24

---

* Previously presented Ph1 data
  - Identified target doses ≥ 20 mcg as consistently pharmacodynamically and clinically active
  - Included 7 efficacy-evaluable CM pts
- Tumor PRAME expression evaluated by IHC
- Gene expression in whole blood at baseline evaluated by bulk RNASeq


* 47 monotherapy patients at brenetafusp target dose of ≥ 20 mcg including 40 new patients and follow-up on 7 CM patients previously presented
### CM Demographics and baseline characteristics

**Brentafusp monotherapy and in combination with pembrolizumab**

#### Patients were heavily pre-treated

- All received prior checkpoint inhibitors (CPI)
  - Median 2 prior anti-PD1 regimens
  - 81% prior ipilimumab – nearly all in combination with nivolumab
  - 38% had another IO, in addition to anti-PD1, anti-CTLA4
- Pembro combo pts. more heavily pre-treated
  - Higher percentage with prior BRAFi and primary resistance to anti-PD1

**PRAME expression was high (median H score 215 in monotherapy)**†


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Monotherapy N=47</th>
<th>+ Pembro N=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr – median (range)</td>
<td>64 (31-79)</td>
<td>65 (24-78)</td>
</tr>
<tr>
<td>Female – n (%)</td>
<td>19 (40%)</td>
<td>4 (44%)</td>
</tr>
<tr>
<td>ECOG status 0 – n (%)</td>
<td>27 (57%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td><strong>Baseline disease status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III/IV M1a</td>
<td>3 (6%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Stage IV M1b/c/d</td>
<td>44 (94%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Brain metastasis – n (%)</td>
<td>10 (21%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Liver metastasis – n (%)</td>
<td>21 (45%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Sum of target lesions*, mm – median (range)</td>
<td>84 (14-309)</td>
<td>73 (24-117)</td>
</tr>
<tr>
<td><strong>Prior therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td># lines – median (range)</td>
<td>2 (1-9)</td>
<td>4 (1-7)</td>
</tr>
<tr>
<td>Anti-PD1</td>
<td>47 (100%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Primary resistant† – n (%)</td>
<td>14 (30%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Anti-CTLA4</td>
<td>38 (81%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>BRAF inhibitor</td>
<td>7 (15%)</td>
<td>4 (44%)</td>
</tr>
<tr>
<td><strong>PRAME status (IHC)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive‡</td>
<td>42 (89%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>H-score§ – median</td>
<td>215</td>
<td>155</td>
</tr>
</tbody>
</table>

Includes patients receiving target doses ≥20mcg

* Sum of target lesions at baseline; one pembrolizumab combo pt had non-target lesions only
† Primary resistant to anti-PD1: progressed within 6 months of starting first anti-PD1-containing regimen
‡ PRAME positive group for efficacy analysis includes H-score ≥1 and pts with unknown PRAME IHC results; maximum H-score 300
§ Amongst IHC evaluable pts (n=38 mono, n=5 combo)
Brenetafusp monotherapy was well tolerated

TRAE in ≥ 15% of patients (N=47)

<table>
<thead>
<tr>
<th>Preferred Term (%)</th>
<th>Any grade</th>
<th>Grade 3 / 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY</td>
<td>43 (92%)</td>
<td>19 (40%)</td>
</tr>
<tr>
<td>Cytokine release syndrome*</td>
<td>24 (51%)</td>
<td>-</td>
</tr>
<tr>
<td>Rash (composite)†</td>
<td>23 (49%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>17 (36%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Chills</td>
<td>13 (28%)</td>
<td>-</td>
</tr>
<tr>
<td>Lymphocyte decrease</td>
<td>12 (26%)</td>
<td>11 (23%)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>11 (23%)</td>
<td>-</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (19%)</td>
<td>-</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (15%)</td>
<td>-</td>
</tr>
</tbody>
</table>

* CRS graded per ASTCT 2019 criteria; all other AE per CTCAE v5.0
† Rash is a composite term for a list of skin toxicities of any grade (Nathan et al. 2021)

Other G3 treatment-related adverse events (TRAE, in 1 pt each): anemia, chronic inflammatory demyelinating polyneuropathy, fever, hypotension, hypoxia, pain in extremity, tumor lysis syndrome, urticaria

- Safety consistent with previous report; no new signal with continued dosing
- Most frequent TRAE was G1/G2 CRS, consistent with mechanism
- TRAE frequency and severity attenuated over time
- The only G4 TRAEs were lymphocyte decrease (n=11) / lymphopenia (n=3), transient and related to mechanism
- No severe neutropenia observed
- 1 TRAE resulted in treatment discontinuation
- No treatment-related deaths
Clinical benefit characterized by durable disease control

Brenetafusp monotherapy (n= 36 evaluable*)

PRAME positive group for efficacy analysis includes H-score ≥1 and pts with unknown PRAME IHC results

* 36/47 patients had baseline and at least one tumor assessment on treatment; 10 patients had no evaluable post-baseline tumor scans and 1 had non-target lesions only at baseline.
Clinical benefit characterized by disease control

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>DCR (PR+SD)</th>
<th>PR + SD with confirmed tumor reduction*</th>
<th>ORR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All mono</td>
<td>36</td>
<td>56%</td>
<td>28%</td>
<td>11%</td>
</tr>
<tr>
<td>PRAME+</td>
<td>31</td>
<td>58%</td>
<td>32%</td>
<td>13%</td>
</tr>
<tr>
<td>PRAME-</td>
<td>5</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Reduction in tumor burden is associated with clinical benefit across ImmTAC platform

Nathan NEJM¹; Middleton CCR²; see ASCO 2024 poster #9529

---

PRAME positive group for efficacy analysis includes H-score ≥1 and pts with unknown PRAME IHC results

* Defined as patients with PR + patients SD or better who have tumor reduction that is confirmed in a subsequent scan after at least 4 weeks with no progressive disease in between

Tumor reduction observed only in PRAME+ pts

Brenetafusp monotherapy (n= 36 evaluable)

PRAME positive group for efficacy analysis includes H-score ≥1 and pts with unknown PRAME IHC results
Tumor reduction observed in patients with high tumor burden
Brenetafusp monotherapy (n= 36 evaluable)
Tumor reduction observed in patients with liver and brain mets
Brenetafusp monotherapy (n= 36 evaluable)
ctDNA molecular response in 42% of PRAME+ patients

Brenetafusp monotherapy (n=28 ctDNA evaluable*)

- Trend for longer PFS (HR 0.5) and OS (HR 0.3) in molecular responders
- Molecular response in patients with PR, SD and PD
- 4 pts have ≥99% ctDNA reduction

PRAME positive group includes H-score ≥1 and pts with unknown PRAME IHC results
* ctDNA evaluable defined as ≥1 mutation detected at baseline at >0.3% VAF AND data from at least one on-treatment timepoint up to week 9; n=28 ctDNA evaluable, best response by week 9
† Molecular response defined as ≥0.5log (≥68%) ctDNA reduction by week 9
Promising initial PFS and OS, enriched in PRAME+ pts
Brenetafusp monotherapy (n= 47)

Progression free survival

Overall survival

<table>
<thead>
<tr>
<th></th>
<th>mPFS mo (95% CI)</th>
<th>No. at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All mono</td>
<td>3.3 (2.1-5.6)</td>
<td>42 16 10 4 4 1 1 1 1 0</td>
</tr>
<tr>
<td>PRAME+</td>
<td>4.2 (2.1-6.1)</td>
<td>42 31 26 13 10 7 3 2 2 2 1 0</td>
</tr>
<tr>
<td>PRAME-</td>
<td>2.1 (1.3-NC)</td>
<td>5 2 1 0</td>
</tr>
</tbody>
</table>

6-mo OS rate

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>No. at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All mono</td>
<td>87%</td>
<td>42 16 10 4 4 1 1 1 1 0</td>
</tr>
<tr>
<td>PRAME+</td>
<td>95%</td>
<td>42 31 26 13 10 7 3 2 2 2 1 0</td>
</tr>
<tr>
<td>PRAME-</td>
<td>40%</td>
<td>5 2 1 0</td>
</tr>
</tbody>
</table>

PRAME positive group includes H-score ≥1 and pts with unknown PRAME IHC results

Median follow up 7.8 mos
Initial data for anti-PD1 combination shows well tolerated profile

Brenetafusp + pembrolizumab dose escalation safety cohort (n=9 CM patients)

- **Primary goal to demonstrate safety in combination**
  - Safety profile similar to each agent alone
  - 1 DLT (transaminitis) in patient with previous CPI-induced autoimmune hepatitis
- Safety profile supported by additional 12 pts dosed in combination across multiple tumors
- Secondary goal was to evaluate initial efficacy
  - 4 of 7 efficacy evaluable pts had disease control, including 1 unconfirmed PR still ongoing
  - 3 of 4 ctDNA evaluable pts had molecular response

<table>
<thead>
<tr>
<th>Preferred Term (%)</th>
<th>Any grade (N=9)</th>
<th>Grade 3 / 4 (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY</td>
<td>9 (100%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Cytokine release syndrome†</td>
<td>5 (56%)</td>
<td>-</td>
</tr>
<tr>
<td>Rash (composite)‡</td>
<td>5 (56%)</td>
<td>-</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (33%)</td>
<td>-</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (33%)</td>
<td>-</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Aspartate aminotransferase incr</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Alanine aminotransferase incr</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (22%)</td>
<td>-</td>
</tr>
</tbody>
</table>

† CRS graded per ASTCT 2019 criteria
‡ Rash is a composite term for a list of skin toxicities of any grade (Nathan et al. 2021)

**Median follow up 3.5 mos**
Phenotype of peripheral blood T cells, which are recruited by brenetafusp, may be important for clinical activity

**Hypothesis:**
Specific T cell subsets in the blood may be associated with brenetafusp benefit

**Method:**
- RNAseq whole blood at baseline
- Analyzed key T cell subsets:
  - Naïve /stem cell memory T cell (T\text{scm})
  - Effector
  - Exhausted
  - Regulatory

*Naïve T/T\text{scm} have been associated with anti-tumor activity of other T cell therapies¹.*

---

Novel T cell fitness (TCF) signature associated with brenetafusp benefit

TCF higher in earlier lines of therapy and highly correlated with naïve/T<sub>scm</sub> cells

**Monotherapy benefit by TCF signature**

<table>
<thead>
<tr>
<th></th>
<th>High*</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>41†</td>
<td>20</td>
</tr>
<tr>
<td>n</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>mPFS</td>
<td>6 mo</td>
<td>2 mo</td>
</tr>
<tr>
<td>ORR</td>
<td>19%</td>
<td>0%</td>
</tr>
<tr>
<td>DCR</td>
<td>69%</td>
<td>42%</td>
</tr>
</tbody>
</table>

* For exploratory analysis, 'high' defined as ≥ median gene expression signature level

**TCF signature, by line of therapy**

Other gene signatures, including T effector and exhausted T cell phenotype, not associated with clinical benefit (data not shown)

† 41 monotherapy CM patients had baseline TCF and were evaluable for tumor assessment on therapy;
‡ 42 monotherapy CM and 6 pembrolizumab combination patients had baseline T cell fitness evaluated
Conclusions

- Brenetafusp is well tolerated
  - Most frequent TRAE is reversible and manageable CRS (Grade 1-2)
  - Brenetafusp can be safely combined with anti-PD1
- Promising monotherapy activity in heavily pretreated CM supports a PFS endpoint
  - Enriched in PRAME+: DCR (58%), confirmed tumor reduction (32%), molecular response (42%) and mPFS (4.2mo)
  - These endpoints best capture brenetafusp benefit and are consistent across ImmTAC platform\(^1\)\(^-\)\(^3\) (2024 ASCO poster #9529)
- T cell fitness signature associated with brenetafusp benefit and higher in earlier lines of therapy
  - This association emerging across ImmTAC platform and reported for other T cell therapies\(^4\)
- Data support Ph3 brenetafusp + nivolumab in 1st line mCM (PRISM-MEL301; NCT06112314)

PRISM-MEL301: First-line advanced CM Phase 3

→ **Key inclusion criteria**
  - Previously untreated, advanced melanoma
  - HLA-A*02:01
  - No prospective PRAME testing

→ **Stratification factors**
  - AJCC M stage
  - Prior anti-PD1 adjuvant therapy
  - BRAF V600 status

**Key endpoints**
→ Primary: PFS by BICR
→ Secondary: OS, ORR
→ Exploratory: ctDNA

Initial randomization includes comparison of two brenetafusp regimens (~90 patients or 30/arm)

(PRISM-MEL301; NCT06112314); see ASCO 2024 TiP poster #TPS9602

* Use of nivolumab or nivolumab + relatlimab as control will be country specific
Thank you to all patients, their families and their caregivers who were involved in this global clinical trial & all investigators and their teams

- **Omid Hamid**
  The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate

- **Takami Sato**
  Thomas Jefferson University Hospitals

- **Diwakar Davar**
  University of Pittsburgh Medical Center

- **Benjamin Izar**
  Columbia University Medical Center

- **Daniel Olson**
  University of Chicago, Comprehensive Cancer Center

- **Claire Friedman**
  Memorial Sloan Kettering Cancer Center

- **Vincent Ma**
  University of Wisconsin Carbone Cancer Center

- **Peter Lau**
  Linear Clinical Research, Harry Perkins Institute for Medical Research, Nedlands, WA, Australia

- **Georgina Long**
  Linear Clinical Research, Harry Perkins Institute for Medical Research, Nedlands, WA, Australia

- **Oliver Bechter**
  UZ Gasthuisberg - Katholieke University Leuven

- **Bart Neyns**
  Universitair Ziekenhuis

- **Gennaro Daniele**
  Fondazione Policlinico Universitario Agostino Gemelli IRCCS

- **Juanita Lopez**
  Royal Marsden NHS Foundation Trust and Institute of Cancer Research

- **Anja Williams**
  Sarah Cannon Research Institute, London

- **Fiona Thistlethwaite**
  The Christie NHS Foundation and University of Manchester

- **Heather Shaw**
  University College London

- **Mark Middleton**
  University of Oxford

- **Catherine Han**
  New Zealand Clinical Research – Auckland

- **Piotr Tomczak**
  Cetrum Medyczne Pratia Poznan

- **Dong-Wan Kim**
  Seoul National University Hospital

- **Dae Ho Lee**
  Asan Medical Center

- **Celeste Lebbe**
  Université Paris Cité, Hôpital Saint-Louis, INSERM
**Multiple lines of evidence supports 1L Ph3 combo (nivo + brene)**

**High monotherapy DCR in 2L+ | ImmTAC activity higher in 1L | Combination with nivolumab in 1L**

<table>
<thead>
<tr>
<th></th>
<th>2L+</th>
<th>1L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mPFS 3.7m</td>
<td>4.6m</td>
</tr>
<tr>
<td></td>
<td>3.1m 3.2m</td>
<td>10.2m</td>
</tr>
<tr>
<td></td>
<td>HR=1.0, n.s.</td>
<td>?</td>
</tr>
<tr>
<td>DCR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR/CR</td>
<td>38% 47%</td>
<td>49% 60%</td>
</tr>
<tr>
<td>SD</td>
<td>28% 20%</td>
<td>33% 16%</td>
</tr>
<tr>
<td></td>
<td>27% 31%</td>
<td>43% 17%</td>
</tr>
<tr>
<td>mPFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemo 133 pts</td>
<td>Nivo 359 pts</td>
</tr>
<tr>
<td></td>
<td>Nivo 272 pts</td>
<td>Rela + Nivo 355 pts</td>
</tr>
<tr>
<td></td>
<td>Rela + Nivo 163 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ph2 CM037¹</td>
<td>Ph1/2 Rela-020²</td>
</tr>
<tr>
<td></td>
<td>Ph1/2 F106C-101</td>
<td>PRAME (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>36 pts</td>
<td>31 pts</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td></td>
</tr>
<tr>
<td>Brene monotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ph3 Rela-047³</td>
<td>Ph3 PRISM-MEL301</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior PD-1</td>
<td>0% 10%</td>
<td>0% 16%</td>
</tr>
<tr>
<td>Prior CTLA-4</td>
<td>100% 100%</td>
<td>100% 81%</td>
</tr>
</tbody>
</table>

Melanoma franchise
TEBE-AM trial now conducted as a Ph3
All patients randomized to date included in ITT following FDA consultation

<table>
<thead>
<tr>
<th>Original Design (Ph2/3)</th>
<th>Updated Design (Ph3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase 2</strong></td>
<td><strong>Phase 3</strong></td>
</tr>
<tr>
<td>KIMMTRAK</td>
<td>KIMMTRAK + anti-PD-1</td>
</tr>
<tr>
<td>KIMMTRAK + anti-PD-1</td>
<td>KIMMTRAK + anti-PD-1</td>
</tr>
<tr>
<td><strong>Straight to follow up</strong></td>
<td><strong>Straight to follow up</strong></td>
</tr>
</tbody>
</table>

**Phase 3 endpoint**

- OS

**Eligibility**

- Prior anti-PD1, ipilimumab, BRAF (if mutation positive)
- Unchanged from original design

**Experimental arms**

- KIMMTRAK or KIMMTRAK + anti-PD1
- KIMMTRAK and KIMMTRAK + anti-PD1

- **Leverages recent rapid accrual**
- **More robust evaluation of two KIMMTRAK regimens:** As monotherapy and as anti-PD1 combination
- **Faster time to final OS analysis** since all patients randomized to date to be included
Building ImmTAC melanoma franchise with three Phase 3 trials

**Uveal Melanoma**

- **Phase 3**
  - KIMMTRAK® ATOM
  - To start 2H’24

**Cutaneous Melanoma**

- **Phase 3**
  - Brenetal fus + Nivolumab PRISM-MEL-301
    - Enrolling
  - KIMMTRAK® ± Pembrolizumab TEBE-AM
    - Enrolling
Q&A Session

Bahija Jallal
PhD
Chief Executive Officer

Brian Di Donato
Chief Financial Officer and Head of Strategy

David Berman
MD, PhD
EVP, Research and Development

Ralph Torbay
Head of Commercial

Mohammed Dar
MD
SVP, Clinical Development and Chief Medical Officer

Koustubh Ranade
PhD
SVP, Translational Medicine