INTERIM ANALYSIS OF A REGISTRATION-ENABLING STUDY OF PIVEKIMAB SUNIRINE (PVEK, IMGN632) A CD123-TARGETING ANTIBODY-DRUG CONJUGATE, IN PATIENTS WITH BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM (BPDCN)

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DISCLOSURES

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Background

- Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare, aggressive hematologic malignancy derived from myeloid dendritic cell precursors with skin, lymph node, blood, CNS, and bone marrow involvement
  - BPDCN may arise de-novo or in the context of a prior or concomitant hematologic malignancy (PCHM)
- CD123 (IL-3Rα) is ubiquitously expressed in BPDCN blasts but has limited expression on normal tissues\(^1,2\)
- Based on the favorable safety and clinical activity of pivekimab sunirine (IMGN632, PVEK) in patients with relapsed or refractory (R/R) BPDCN, PVEK was granted FDA Breakthrough Therapy Designation in October 2020\(^3\)
- Here we report an interim analysis of safety and anti-BPDCN activity data from a phase 2 study in adult patients with frontline or R/R BPDCN

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Pivekimab Sunirine (PVEK) Mechanism of Action

- PVEK is a first-in-class antibody-drug conjugate (ADC) comprising a high-affinity CD123 antibody, cleavable linker, and an indolinobenzodiazepine pseudodimer (IGN) payload.

- The IGN payload alkylates DNA and causes single strand breaks without crosslinking. IGNs are designed to have high potency against tumor cells, while demonstrating less toxicity to normal marrow progenitors than other DNA-targeting payloads\(^1\).

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Study Design and Objectives

CADENZA (IMGN632-801): Open-label, multicenter, phase 2 study (NCT03386513)

Patients with R/R BPDCN who have received 1-3 prior systemic therapies

Patients with frontline BPDCN who have not received prior systemic therapy

0.045 mg/kg PVEK IV on Day 1 of a 21-day cycle as a <30-minute outpatient infusion

CNS prophylaxis recommended
Patients may receive HSCT as consolidation

Key Inclusion Criteria
- Patients ≥18 years old
- Frontline or R/R BPDCN
- Any CD123 positivity on flow cytometry or IHC
- Frontline patients may have received local therapy (radiotherapy, surgical excision, photodynamic therapy)

Key Exclusion Criteria
- Patients with history of veno-occlusive disease
- Active CNS involvement; R/R patients with history of CNS must have been treated locally and have at least 1 lumbar puncture with no evidence of CNS disease

Primary Endpoint
- CR +CRc rate

Key SecondaryEndpoints
- Duration of complete response (CR+CRc)
- Overall response rate (ORR)
### Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Frontline BPDCN N=30</th>
<th>R/R BPDCN N=49</th>
</tr>
</thead>
</table>
| **Age, %**
- Median (range), y  
  ≥ 65y                  | 74 (48-84) 90        | 69 (19-82) 59 |
| **Gender, %**
- Male                     | 80                   | 82            |
- Female                   | 20                   | 18            |
| **Disease, %**
- Skin                     | 93                   | 65            |
- Bone marrow              | 43                   | 47            |
- Nodal disease (PET/CT scan) | 47               | 41            |
| **Baseline status, %**
- Primary refractory       | -                    | 43            |
- First relapse             | -                    | 33            |
- Second or greater relapse | -                    | 25            |
| **Prior therapy, %**
- Non-intense (e.g., VEN+/-HMA, CVP, steroids) | -           | 74            |
- Tagraxofusp              | -                    | 43            |
- Intense (e.g., HyperCVAD, FLAG, CHOP) | -      | 55            |
- Stem cell transplant (14 allo, 2 auto) | -           | 33            |
- Local radiotherapy       | 7                    | 18            |
| **Number of prior lines of treatment**
- 1                        | -                    | 53            |
- 2                        | -                    | 27            |
- 3+                       | -                    | 18            |

*Patients can have multiple sites of disease involvement

Prior therapy types are not mutually exclusive

CT, computerized tomography; CVP, cyclophosphamide/vincristine/prednisone; HMA, hypomethylating agent; PET, positron emission tomography; R/R, relapsed or refractory; VEN, venetoclax; y, years.
Safety Overview

### All Frontline and R/R BPDCN Patients (N=79)

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (TEAEs)*</th>
<th>All Grades ≥ 15%</th>
<th>≥ 3 Grade</th>
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<th>All Grades ≥ 15%</th>
<th>≥ 3 Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral edema</td>
<td>46%</td>
<td>10%</td>
<td>Headache</td>
<td>19%</td>
<td>4%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>27%</td>
<td>19%</td>
<td>Neutropenia</td>
<td>18%</td>
<td>17%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>25%</td>
<td>4%</td>
<td>Diarrhea</td>
<td>17%</td>
<td>0%</td>
</tr>
<tr>
<td>Infusion-related reactions (IRRs)</td>
<td>25%</td>
<td>4%</td>
<td>Hypokalemia</td>
<td>17%</td>
<td>3%</td>
</tr>
<tr>
<td>Constipation</td>
<td>23%</td>
<td>0%</td>
<td>Dyspnea</td>
<td>15%</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea</td>
<td>22%</td>
<td>0%</td>
<td>Hyperglycemia</td>
<td>15%</td>
<td>6%</td>
</tr>
<tr>
<td>Anemia</td>
<td>20%</td>
<td>8%</td>
<td>Pyrexia</td>
<td>15%</td>
<td>1%</td>
</tr>
</tbody>
</table>

*Regardless of attribution to PVEK

BPDCN, blastic plasmacytoid dendritic cell neoplasm; R/R, relapsed or refractory.
Safety Overview

Pertinent Less Frequent AEs

- Liver-related AEs:
  - ALT/AST/TBILI laboratory elevations grade 3 in 3%/3%/1%; no grade 4 or 5 events
  - 1 DLT (Grade 3 ALT, duration 7 days)
  - Reversible VOD all grades 4% (3/79); grade 3 in 1% (n=1); no grade 4 or 5 events
    - 1 patient proceeded to transplant without hepatic complications
  - Hypoalbuminemia all grade 13%; grade 3 in 3% (n=2); no grade 4 or 5 events
  - No capillary leak syndrome (CLS) events were reported

- Discontinuations due to PVEK related AEs: 3%
- 30-day mortality rate:
  - Frontline patients: 0%
  - R/R patients: 4% (2 deaths due to disease progression)
**Response Data in Frontline BPDCN**

ORR = CR+CRc+CRh+CRi+PR  
Composite CR = CR+CRc+CRh+CRi

<table>
<thead>
<tr>
<th>Frontline patients (N=30)</th>
<th>ORR</th>
<th>Composite CR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Response rate</strong></td>
<td>80% (24/30)</td>
<td>73% (22/30)</td>
</tr>
<tr>
<td>Time to first response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range), months</td>
<td>1.3 (0.5-3.5)</td>
<td>1.5 (0.5-4.6)</td>
</tr>
</tbody>
</table>

- 9 patients (30%) were bridged to allogeneic stem cell transplant
Due to early censoring events, the current duration of response (DOR) and duration of composite complete remission (DOCR) estimates are immature.

- Median DOR was 12.7 months (95% CI 3.7-13.5) (including post-transplant durability)
- Median DOCR was 10.3 months (95% CI 3.7-12.9) (including post-transplant durability)
In patients with bone marrow involvement at baseline, 100% (13/13) of patients achieved bone marrow remission (<5% blasts).

Of these 11 of 13 patients achieved an overall response (composite CR+PR).

aPatients with >5% bone marrow blasts at baseline only.
Response Seen in Frontline Patient

- 66-year-old male
- Skin mSWAT 88.5 to 0 (EOC3), residual non-BPDCN hyperpigmentation
- Bone marrow 62% to 5% (EOC3), negative for BPDCN
- Achieved a CRc and bridged to SCT

Informed consent was obtained from the patient for use of these images.

BPDCN, blastic plasmacytoid dendritic cell neoplasm; CCR, composite complete response; EOC3, end of cycle 3; mSWAT, modified severity-weighted assessment tool; SCT, stem cell therapy.
**Response Data in R/R BPDCN**

<table>
<thead>
<tr>
<th>R/R patients (N=49)</th>
<th>ORR</th>
<th>Composite CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All R/R patients</td>
<td>33% (16/49)</td>
<td>20% (10/49)</td>
</tr>
<tr>
<td>Patients who received prior tagraxofusp (n=21)</td>
<td>33% (7/21)</td>
<td>19% (4/21)</td>
</tr>
<tr>
<td>Patients who had prior SCT (n=16)</td>
<td>50% (8/16)</td>
<td>31% (5/16)</td>
</tr>
<tr>
<td>Time to first response in all R/R patients</td>
<td>Median (range), months</td>
<td>1.3 (0.6-3.7)</td>
</tr>
</tbody>
</table>

ORR = CR + CRc + CRh + CRi + PR

Composite CR = CR + CRc + CRh + CRi

- 4 patients (8%) were bridged to allogeneic stem cell transplant
- In the 10 patients who did not respond to prior tagraxofusp, 3 of the 10 had a response to PVEK
Due to early censoring events, the current duration of overall response (DOR) and composite complete remission (DOCR) estimates are immature.

- Median DOR was 7.1 months (95% CI 1.8-NE) (including post-transplant durability)
- Median DOCR was 9.2 months (95% CI 0.8-NE) (including post-transplant durability)
Conclusions

- PVEK demonstrates compelling clinical activity and tolerable safety in frontline and R/R BPDCN
  - The safety profile was manageable with mostly low-grade peripheral edema and infusion-related reactions
  - PVEK monotherapy leads to high composite CR rates (73%) in frontline BPDCN, as well as durable responses in R/R patients (DOR 7.1 months), including those treated with prior tagraxofusp

- Enrollment continues in the pivotal frontline BPDCN patient cohort (NCT03386513)
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