



Our STN: BLA 125832/0

**MID-CYCLE COMMUNICATION
SUMMARY**
May 09, 2025

Precigen, Inc.
Attention: Amy Lankford, PhD
SVP, Head of Clinical Operations & Reg Affairs
20358 Seneca Meadows Parkway
Germantown, MD 20876

Dear Dr. Lankford:

Attached is a copy of the summary of your May 6, 2025, Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the Teleconference. If your understanding of the Teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to STN BLA 125832/0 in your future submissions related to zopapogene imadenovec [PAPZIMEOS].

If you have any questions, please contact Helen Sansone at (240) 549-2276 or Helen.Sansone@fda.hhs.gov.

Sincerely,

Mara Miller, MA
Director
Division of Review Management and Regulatory Review 2
Office of Review Management and Regulatory Review
Office of Therapeutic Products
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA 125832/0

Product Name: zopapogene imadenovec [PAPZIMEOS]

Proposed Indication for Use: For the Treatment of adults with Recurrent Respiratory Papillomatosis (under review)

Applicant: Precigen, Inc.

Meeting Date & Time: Tuesday, May 6, 2025; 1:00pm – 1:30pm ET

Committee Chair: Sukyoung Sohn, PhD

RPM: Helen Sansone

Attendees:

Andrew Byrnes, PhD, CBER/OTP/OGT
Colleen Caldwell, MS, MPH, CBER/OTP/ORMRR
Char-Dell Edwards, BS, CBER/OCBQ/DIS
Alifiya Ghadiali, PhD, CBER/OCBQ/DMPQ
Denise Gavin, PhD, CBER/OTP/OGT
Joydeep Ghosh, PhD, CBER/OTP/OGT
Andrew Harmon, PhD, CBER/OTP/OGT
Alicia Howard, CBER/OCBQ/DBSQC
Yuqun Abigail Luo, PhD, CBER/OBPV/DB
Ou Ma, PhD, CBER/OCBQ/DMPQ
Mara Miller, MA, CBER/OTP/ORMRR
Helen Sansone, CBER/OTP/ORMRR
Seth Schulte, MS, CBER/OCBQ/DBSQC/LMIVTS
John Scott, PhD, MA, CBER/OBPV/DB
Shalini Seetharaman, MS, CBER/OTP/ORMRR
Muhammad Shahabuddin, PhD, CBER/OCBQ/DBSQC
Anurag Sharma, PhD, CBER/OTP/OGT
Prateek Shukla, MD, CBER/OTP/OCE/DCEGM
Sukyoung Sohn, PhD, CBER/OTP/OGT
Hsiaoling Wang, CBER/OCBQ/DBSQC
Jianyang Wang, PhD, CBER/OTP/OGT
Yakun Wang, PhD, CBER/OBPV/DB
Lihan Yan, PhD, CBER/OBPV/DB

Applicant Attendees:

Doug Brough, Senior Vice President, Head of Research
Bryan Butman, Senior Vice President, Head of CMC
Shanti Ghosh, Executive Director, Regulatory Affairs
Amy Lankford, Senior Vice President, Head of Clinical Operations & Regulatory Affairs
Jacob Pattasseril, Executive Director, Gene Therapy Manufacturing
Helen Sabzevari, President and Chief Executive Officer
Rutul Shah, Chief Operating Officer
James Wong, Executive Director, Quality Control

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.

- The review of the BLA is on-going. No significant issues/major deficiencies have been identified at this time.

Meeting Discussion for Agenda item 1:

There was no discussion of this question during the meeting.

2. Information regarding major safety concerns.

- At this time, no major safety concerns have been identified.

Meeting Discussion for Agenda item 2:

There was no discussion of this question during the meeting.

3. Preliminary Review Committee thinking regarding a.) risk management, b) the potential need for any post-marketing requirement(s) (PMRs), and/or safety-related PMCs, and c.) the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk.

- Risk Evaluation and Mitigation Strategies (REMS) are not anticipated at this time.
- The review of the BLA is on-going. A PMR related to the confirmatory study for this accelerated approval submission is expected. If additional PMRs are anticipated, we will notify the applicant.
- We have identified the following potential post-marketing commitments (PMCs):
 - 1) Final report for the Drug Product (DP) process performance qualification (PPQ) including additional PPQ runs (i.e., (b) (4) [REDACTED])
 - 2) Final report for the (b) (4) [REDACTED] assessment in the DP.
 - 3) Reassessment of the acceptance criteria for commercial DP release after manufacturing additional lots.

Meeting Discussion for Agenda item 3:

There was no discussion of this question during the meeting.

4. Any information requests sent, and responses not received.

- On April 29, 2025, DBSQC requested the applicant to perform routine lot release testing following the guidance in (b) (4) to submit method suitability results using at least (b) (4) or justify a (b) (4) volume of test sample used for routine sterility lot release testing, and provide a risk assessment indicating the (b) (4) sample test volume will have little to no impact on the assurance provided by the test method. Responses are due by May 5, 2025.
- On April 30, 2025, Clinical requested updated information for all patients enrolled in study PRGN-2012-201 at time of data cutoff of March 20, 2025; requested total number of patients who have been evaluated at month 12, month 24, and 3 years/end of study. In addition, requested an updated table of all subjects enrolled in the study indicating current status in the ongoing study and the number of surgical interventions prior to and post treatment at multiple timepoints. Responses are due by May 5, 2025.

Meeting Discussion for Agenda item 4:

Precigen, Inc. submitted responses to the DBSQC information request (dated April 29, 2025) and the Clinical information request (dated April 30, 2025) on May 05, 2025, in amendment BLA 125812/0.31 (SN0032). The review is ongoing.

5. Any new information requests to be communicated.

- As the review continues, new information requests will be conveyed as needed.
- The following statistical information request is planned to be sent to applicant in the near future:

You counted the surgery on Day 1 of the study as one of the baseline surgeries and used these baseline numbers in the efficacy analyses. This approach leads to the baseline number of surgeries always being one more than that in the EEP of the same duration in the absence of any treatment effect. While it is reasonable to include a Day 1 surgery for the study design, the addition of this surgery towards to baseline surgery count for efficacy comparison with EEP leads to bias. We request that you perform and submit results of the following efficacy analyses by excluding the Day 1 surgery from the number of baseline surgeries:

- a) Please submit the reanalysis of Figure 3 (CSR, p.64), by decreasing all baseline number of surgeries by 1. In addition,

please submit a similar figure with the subjects ordered chronologically by the time of their Day 1 surgery.

- b) Please submit the reanalysis of Table 13 (CSR, p.63) and Table 14 (CSR, p.65), which present various comparisons between the baseline and EEP surgery counts.

Meeting Discussion for Agenda item 5:

FDA explained that the statistical review has identified some technical issues that impact the accuracy of the treatment effect description with the current analyses. At this time, these issues do not impact the conclusion on efficacy qualitatively. FDA requested the re-analyses to improve the accuracy. FDA suggested an informal teleconference after the Mid-Cycle meeting to further clarify and discuss the basis of this request.

Precigen agreed to have an informal teleconference for further discussion.

6. Proposed date(s) for the Late-Cycle meeting (LCM).

- The Late Cycle Meeting between you and the Review Committee is currently scheduled for **June 12, 2025 from 1:00 pm to 2:00 pm ET.**
- We intend to send the Late Cycle meeting materials to you approximately 10 days in advance of the meeting.

Meeting Discussion for Agenda item 6:

There was no discussion of this question during the meeting.

7. Updates regarding plans for the AC meeting.

- There are currently no plans for an AC meeting.

Meeting Discussion for Agenda item 7:

There was no discussion of this question during the meeting.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

Milestones	Date
Communicate Anticipated PMRs	July 16, 2025
Communicate PMCs and Start Labeling Negotiations	July 28, 2025
PDUFA Date:	August 27, 2025 (Wednesday)

Meeting Discussion for Agenda item 8:

There was no discussion of this question during the meeting.

9. Discuss status of inspections (GMP, BiMo, GLP) including issues identified that could prevent approval. **Note:** Ensure notification of intent to inspect manufacturing facilities has been issued.
- The clinical investigator and Sponsor site inspections have been completed. The Establishment Inspection Report (EIR) is pending submission for BIMO review and final classification.
 - The Pre-License Inspection (PLI) of (b) (4) facility in (b) (4) in support of PRGN-2012 Drug Product manufacturing was completed on (b) (4). An FDA Form 483 was issued at the conclusion of the PLI. The PLI classification is pending.
 - The PLI of the Precigen facility in Germantown, Maryland in support of PRGN-2012 Drug Substance manufacturing is being conducted from April 28, 2025 to May 2, 2025.

Meeting Discussion for Agenda item 9:

There was no discussion of this question during the meeting.