Food and Drug Administration
Center for Drug Evaluation and Research
Final Summary Minutes of the Medical Imaging Drugs Advisory Committee Meeting

Location: All meeting participants were heard, viewed, captioned, and recorded for this advisory committee meeting via an online teleconferencing and/or video conferencing platform.

Topic: The Committee discussed efficacy and safety data submitted in support of a new drug application (NDA) 214511 for pegulicianine for injection, the optical imaging drug constituent of a drug/device combination product, submitted by Lumicell, Inc. The proposed indication for pegulicianine is for use in adults with breast cancer as an adjunct for the intraoperative detection of cancerous tissue within the resection cavity following removal of the primary specimen during lumpectomy surgery.

These summary minutes for the March 5, 2024 meeting of the Medical Imaging Drugs Advisory Committee of the Food and Drug Administration were approved on ____4/1/2024_____.

I certify that I attended the March 5, 2024 meeting of the Medical Imaging Drugs Advisory Committee (MIDAC) of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Jessica Seo, PharmD, MPH	Henry D. Royal, MD
Acting Designated Federal Officer, MIDAC	Chairperson, MIDAC

Final Summary Minutes of the Medical Imaging Drugs Advisory Committee Meeting
March 5, 2024

The Medical Imaging Drugs Advisory Committee (MIDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on March 5, 2024. The meeting presentations were heard, viewed, captioned, and recorded through an online videoconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Lumicell, Inc. The meeting was called to order by Henry D. Royal, MD (Chairperson). The conflict of interest statement was read into the record by Jessica Seo, PharmD, MPH (Acting Designated Federal Officer). There were approximately 232 people online. There was a total of 10 Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda:

The Committee discussed efficacy and safety data submitted in support of a new drug application (NDA) 214511 for pegulicianine for injection, the optical imaging drug constituent of a drug/device combination product, submitted by Lumicell, Inc. The proposed indication for pegulicianine is for use in adults with breast cancer as an adjunct for the intraoperative detection of cancerous tissue within the resection cavity following removal of the primary specimen during lumpectomy surgery.

Attendance:

Medical Imaging Drugs Advisory Committee Members Present (Voting): Kimberly E. Applegate, MD, MS, FACR; Wesley E. Bolch, PhD, FAAPM, FAIMBE; David B. Hackney, MD; Paula M. Jacobs, PhD; M. Elizabeth Oates, MD, FAAWR, FACR; Eben L. Rosenthal, MD; Henry D. Royal, MD (*Chairperson*); Chengjie Xiong, PhD;

Medical Imaging Drugs Advisory Committee Members Not Present (Voting): Peter Herscovitch, MD, FACP, FRCPC, FSNMMI; Steven M. Larson, MD; Rupa M. Sanghani, MD, FACC, FASNC;

Acting Industry Representative to the Committee (Non-Voting): P. LaMont Bryant, PhD (*Acting Industry Representative*)

Temporary Members (Voting): Harold J. Burstein, MD, PhD; Michael C. Dejos, PharmD, MBA; Mark Dykewicz, MD; Melissa Fisher (*Patient Representative*); Paul A. Greenberger, MD; Marie R. Griffin, MD, MPH; A. Marilyn Leitch, MD, FACS; Cynthia (Cindy) Pearson (*Acting Consumer Representative)*; Andrea Richardson, MD, PhD; Steven J. Skates, PhD; Neil Vasan, MD, PhD

FDA Participants (Non-Voting): Charles Ganley, MD; Alex Gorovets, MD; Libero Marzella, MD, PhD; A. Alex Hofling, MD, PhD; Anil Rajpal, MD, MPH; Shane Masters, MD, PhD; Sue-Jane Wang, PhD; Miya Paterniti, MD; Rachel Bean, MD; Steven Bird, PhD, PharmD; Kate Gelperin, MD, MPH; Mallika Mundkur, MD MPH; Cynthia LaCivita, PharmD; Jessica Carr, PhD; Dorian M. Korz, MD; Colin Kejing Chen, PhD; Steven Nagel, MD FACS

Acting Designated Federal Officer (Non-Voting): Jessica Seo, PharmD, MPH

Open Public Hearing Speakers Present: Jay K. Harness, MD, FACS; Diane Bloom; Karen Maness (statement read by Jennifer Montes, MD); Donna-Lynn Dyess, MD, FACS; Donna Huie; Shawna C. Willey, MD, FACS; Patricia Clark, MD, FACS, FSSO; Roberto Diaz, MD, PhD; Jennifer Montes, MD; Irene L. Wapnir, MD (Evolve Pink)

The agenda was as follows:

Call to Order	**Henry Royal, MD** Chairperson, MIDAC
Introduction of Committee and Conflict of Interest Statement	**Jessica Seo, PharmD, MPH** Acting Designated Federal Officer, MIDAC
FDA Introductory Remarks	**A. Alex Hofling, MD, PhD** Deputy Division Director Division of Imaging and Radiation Medicine (DIRM) Office of Specialty Medicine (OSM) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Lumicell, Inc.**
Introduction	**Jorge Ferrer, PhD** Chief Scientific Officer Lumicell, Inc.
Unmet Need	**Kelly Hunt, MD, FACS, FSSO** Professor and Chair Department of Breast Surgical Oncology Division of Surgery MD Anderson Cancer Center President, Society of Surgical Oncologists
Pivotal Study CL0007 Efficacy Results	**E. Shelley Hwang, MD, MPH** Mary and Deryl Hart Distinguished Professor of Surgery Vice Chair of Research Department of Surgery Leader, Breast Cancer Disease Group Duke University and Duke Cancer Institute

APPLICANT PRESENTATIONS (CONT.)

Safety	**Peter Blumencranz, MD, FACS** Medical Director BayCare Oncology Service Line Health System Medical Director The Comprehensive Breast Care Center of Tampa Bay
Allergic Reactions and Hypersensitivity	**Tanya Laidlaw, MD, FAAAAI** Director of Translational Research, Division of Allergy and Clinical Immunology Chief, Section of Clinical and Translational Sciences Division of Allergy and Clinical Immunology Brigham and Women's Hospital Associate Professor Harvard Medical School
Risk Mitigation Strategies	**Jorge Ferrer, PhD**
Clinical Perspective	**Barbara Smith, MD, PhD** Director, Breast Program Massachusetts General Hospital Massachusetts General Hospital Trustees Chair in Breast Surgery Professor of Surgery Harvard Medical School
Clarifying Questions to the Applicant	

BREAK

FDA PRESENTATIONS

Clinical Overview	**Shane Masters, MD, PhD** Clinical Team Leader DIRM, OSM, OND, CDER, FDA
Statistical Designs and Review of Efficacy Results	**Sue-Jane Wang, PhD** Deputy Division Director Division of Biometrics 1 Office of Biostatistics Office of Translational Sciences CDER, FDA
Risk Management Considerations	**Anil Rajpal, MD, MPH** Deputy Division Director for Safety DIRM, OSM, OND, CDER, FDA

FDA PRESENTATIONS (CONT.)

Clarifying Questions to FDA

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee — **A. Alex Hofling, MD, PhD**

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion (cont.)

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss whether the observed performance of pegulicianine for patient-level detection of residual cancer, tissue-level sensitivity, and tissue-level specificity provide sufficient evidence of effectiveness.

   Committee Discussion*: The Committee members were in general agreement that there was a modest overall benefit observed with use of pegulicianine, as it met its prespecified endpoints for patient-level detection of residual cancer and tissue-level specificity, but did not meet its tissue-level sensitivity goal. Some members pointed out that even small improvements can be valuable to patients with cancer, and acknowledged that while pegulicianine shows promise, it was not considered a "home run" or a "magical" solution, but rather an incremental benefit that is an important step forward in breast cancer diagnostics. Other members agreed there is a potential to observe better performance of pegulicianine with increased use and improved proficiency and technique among surgeons. One member stressed the need to consider the impact on individual patients and their families when evaluating the effectiveness of medical interventions. Another member expressed concern with setting a precedent for use of tissue-level metrics to support effectiveness. Other members raised concerns regarding the significance of the observed benefits, with emphasis on the relatively small number of patients who avoided a second surgery. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION:** Discuss the risk of serious hypersensitivity reactions associated with pegulicianine and the adequacy of risk mitigation and assessment strategies under consideration.

   In discussing the risk of serious hypersensitivity reactions associated with pegulicianine and the adequacy of risk mitigation and assessment strategies under consideration, Committee members were in overall agreement that adverse reactions are a concern. However, the majority of participants voiced that given the pre-surgical setting in which the patients would be administered the drug, the risk of hypersensitivity reactions is manageable and does not outweigh incremental benefits associated with pegulicianine. One member raised concerns about the number of serious adverse reactions observed in the trial relative to the number of patients benefiting from the treatment, and there was general agreement that additional safety data collection through a post-marketing study would be valuable to better understand the incidence of adverse reactions. Most committee members did not support the implementation of a Risk Evaluation and Mitigation Strategy (REMS), considering it unnecessary for this particular drug. Suggestions for risk mitigation included labeling recommendations for monitoring of patients during and after infusion and immediate access to medical care in case of adverse reactions. The possibility of pretreatment with antihistamines was discussed, with one member suggesting it could be considered based on individual patient factors and clinical judgment. Please see the transcript for details of the Committee's discussion.

3. **VOTE:** Do the benefits of pegulicianine outweigh its risks?
   - If yes, describe the clinically meaningful benefit and the risk mitigation measures that are recommended.
   - If no, provide recommendations for additional data and/or analyses that may support a positive benefit/risk assessment of pegulicianine.

   Vote Result: Yes: 16 No: 2 Abstain: 1

   Committee Discussion:

   The majority of Committee members voted "Yes" on whether the benefits of pegulicianine outweigh its risks. Many members cited the incremental benefits of pegulicianine in detection of residual cancer, as well as the manageable nature of the associated risks, such as hypersensitivity reactions. Suggestions for risk mitigation and assessment included labeling recommendations for monitoring, a post-marketing safety study, and enhanced pharmacovigilance. Some participants expressed concerns about the small absolute benefit and recommended clear patient-level information to set realistic expectations for patients who choose to undergo lumpectomy using pegulicianine.

   Two Committee members voted "No," with one member acknowledging that while pegulicianine appears to detect residual cancer, the clinical utility of pegulicianine is still

questionable without clear evidence of improved patient outcomes. Both Committee members, in addition to the one abstention, advocated for randomized trials to assess the effectiveness of pegulicianine in reducing reoperations.

Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 5:05pm ET.