Food and Drug Administration
Center for Devices and Radiological Health

Summary Minutes of the Anesthesiology and Respiratory Therapy Devices Panel of the Medical Devices Advisory Committee Meeting
June 14, 2018

Location: Gaithersburg Holiday Inn, Grand Ballroom, 2 Montgomery Village Ave., Gaithersburg, MD 20879

Topic: The committee discussed the premarket approval application P170004 for the ELEVAIR™ Endobronchial Coil System which is indicated for bronchoscopic placement of ELEVAIR Coils in patients with severe emphysema (homogeneous and/or heterogeneous) and severe hyperinflation to improve quality of life, lung function, and exercise capacity.

The following is the final report of the Anesthesiology and Respiratory Therapy Devices Panel of the Medical Devices Advisory Committee meeting held on June 14, 2018. A verbatim transcript will be available in approximately six weeks, sent to the Division of Anesthesiology, General Hospital, Respiratory, Infection Control, and Dental Devices and posted on the FDA website at:

MEDICAL DEVICES ADVISORY COMMITTEE PANEL MATERIALS

All external requests for the meeting transcript should be submitted to the CDRH Freedom of Information Office.

The Anesthesiology and Respiratory Therapy Devices Panel of the Medical Devices Advisory Committee of the Food and Drug Administration, Center for Devices and Radiological Health met on June 14, 2018, at the Gaithersburg Holiday Inn, Grand Ballroom, 2 Montgomery Village Ave., Gaithersburg, MD 20879. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and PneumRx, Inc. The meeting was called to order by Steven Nathan, MD (Chairperson). The conflict of interest statement was read into the record by Evella Washington (Designated Federal Officer). There were approximately 125 people in attendance. There were five (5) Open Public Hearing (OPH) speaker presentations.

Issue: The committee discussed the premarket approval application P170004 for the ELEVAIR™ Endobronchial Coil System which is indicated for bronchoscopic placement of ELEVAIR Coils in patients with severe emphysema (homogeneous and/or heterogeneous) and severe hyperinflation to improve quality of life, lung function, and exercise capacity.

Attendance:

MDAC Members Present (Voting): Lonny Yarmus, MD; Hugh Cassiere;

MDAC Member Not Present (Voting): N/A

MDAC Member Present (Non-Voting): *Debra Brown* (Industry Representative); Randy W. Hawkins, MD (Consumer Representative); Teresa R. Barnes (Tosi) (Patient Representative).

Temporary Members (Voting): Karla Ballman, PhD; Alexander C. Chen, MD; Lori E. Dodd, PhD; Jessica Wang Memoli, MD; Steven D. Nathan, MD; Bohdan M. Pichurko, MD; David A. Schoenfeld, PhD; Victor H. van Berkel, MD, PhD.

Designated Federal Officer (Non-Voting): Evella F. Washington

FDA Participants (Non-Voting): Derya Coursey, PhD; Lila Bahadori, MD; Heather Benz, PhD.

Open Public Hearing Speakers: Eileen G. Wilson-Pittsburgh, PA; **Elisa Malanga**-COPD Foundation; **Kathleen Eschenburg**-Willards, MD; **Stephanie Fox-Rawlings, PhD**-National Center for Health Research; **Cindy Gasparo**-Elkton, MD

Agenda:

Call to Order and Introduction of Committee	**Steven Nathan, MD** Chairperson, MDAC ,
Conflict of Interest Statement	**Evella Washington** Designated Federal Officer, MDAC
FDA Introductory Remarks	**None Given**
APPLICANT PRESENTATIONS	**PneumRx, Inc**
ELEVAIR Endobronchial Coil System Introduction	**Julia Anastas, MPH** Vice President, Regulatory Affairs PneumRx, Inc., a BTG International group company
Emphysema Disease Background	**James Donohue, MD** UNC School of Medicine
RENEW Trial Design	**Caire Daugherty, MS** Director, Biostatistics BTG International, Inc.

Development and Effectiveness	**Gerard J. Criner, MD** Founding Chair of Thoracic Medicine and Surgery Temple University
Safety Profile	**David Hahn, MD** Head, PneumRx, Inc. University of Chicago, Pritzker School of Medicine
Post-Market Plan	**Julia Anastas, MPH** Vice President, Regulatory Affairs PneumRx, Inc., a BTG International group company
Patient Preference	**A. Brett Hauber, PhD** Vice President, Health Preference Assessment, RTI Health Solutions University of Washington, School of Pharmacy
Clinical Context	**Frank Sciurba, MD** University of Pittsburgh Medical Center

BREAK

FDA PRESENTATIONS

Study Overview	**Derya Coursey, PhD** Biomedical Engineer/Lead Reviewer DAGRID Office of Device Evaluation
Clinical Review	**Lila Bahadori, MD** Pulmonary Medicine DAGRID Office of Device Evaluation
Patient Preference Information (PPI) Study	**Heather Benz, PhD** Division of Biomedical Physics Office of Science and Engineering Laboratories Center for Devices and Radiological Health

Clarifying Questions to FDA

LUNCH

Open Public Hearing

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion

Questions to the Committee:

1. **DISCUSSION:**

a. The primary effectiveness endpoint evaluated the absolute difference in 6MWT between the treatment and control arm at 12 months. The results showed a median difference of 14.6 meters (adjusted mean difference of 10.2 meters). Please comment on the clinical significance of the observed treatment effect in 6MWT.

Committee Discussion: *The committee acknowledged the statistical significance of this change. However, there was uncertainty around the clinical significance regarding the change observed in 6MWT.*

b. The median percent change in FEV1 at 12 Months was 3.8% in the Coil Treatment group and -2.5% in the Control group, resulting in the median difference between the treatment and control group of 7%. Please comment on the clinical significance of the observed treatment effect in the percent change in FEV1.

Committee Discussion: *The committee acknowledged that 7% may be clinically meaningful and may not be the best surrogate for hyperinflation. It might not fully reflect the benefit or downside of the procedure.*

c. The SGRQ improved by -8.9 points at 12 months in the Coil Treatment Group as compared to the Control group. Please comment on the clinical significance of the SGRQ improvement in the context of an open-label trial and the increase in COPD-related adverse events including hospitalization and emergency room visits for the treatment arm.

Committee Discussion: *The committee acknowledged that the change is SGRQ was clinically significant despite adverse events.*

d. The observed treatment effect for the US subgroup was consistently smaller than that for the OUS subgroup for all the primary and secondary effectiveness endpoints. Also, the treatment by region interaction effects were statistically significant for 6MWT, FEV1 and SGRQ suggesting that pooled results may not be generalizable to the US population. Please comment on pooling of the US and OUS data for an overall assessment of effectiveness of coil treatment for the US population.

Committee Discussion: *The committee acknowledged that the data is poolable.*

2. **DISCUSSION: Multiple subgroup analyses**

   a. Based on the proposed mechanism of action of compression of diseased tissue to allow more normal tissue to expand, the prior NETT study results, and pivotal study results, please comment on the observed treatment effect in the homogeneous and heterogeneous emphysema subpopulations.

   Committee Discussion: *The committee acknowledged that there seems to be difference in treatment response for homogeneous versus heterogenous emphysema patients. There was concern regarding the difference in the results between the pivotal and the crossover group.*

   b. Please comment on the study results in the pivotal and crossover studies based on RV cut-offs (RV≥225 % vs RV<225 %).

Committee Discussion: *The committee acknowledged that there is a difference between* RV≥225 % vs RV<225 %. *There was apparent disparity from the crossover results and the crossover results would be expected to support the pivotal study results.*

3. **DISCUSSION:**

   A central core lab was contracted to review all computed tomography (CT) scans for the pivotal and crossover studies to make recommendations for each site for lobe location of Coil placement. Please comment on the method of centralized scoring and patient selection and how this can be generalized to the real-world use.

Committee Discussion: *The committee acknowledged that although the scoring system was not validated, this would not be an impediment to future use at centers of excellence.*

4. **DISCUSSION:**

   a. Please discuss the safety of the coil treatment with regards to device related mortality, increased risk of COPD exacerbations, pneumonia, and pneumothorax in relation to underlying disease.

Committee Discussion: *The committee acknowledged that if this device is approved, patients should be fully informed regarding the adverse events.*

   b. After the completion of the study, pneumonias were retrospectively adjudicated by the CEC to re-define some of these cases as non-infectious localized tissue reactions to the coils (termed Coil Associated Opacity", or "CAO"). The safety of CAOs has not been established as there were related deaths with autopsy reports with fibrosis at the site of coil implantation. Please discuss the increased risk of pneumonia,

definition and the implication of the CAO with progressive fibrosis in coil treated subjects.

Committee Discussion: *The committee acknowledged that CAO is a concern and if this device is approved, CAO should be monitored through a registry.*

c. There is limited data on the applicant's recommendation for bronchoscopic coil removal within 2 months of deployment. There were no coil removals during the clinical trial and furthermore, the limited autopsy results have shown fibrosis around the coils. Please comment on the coil removal recommendation provided in the labelling for patients with severe emphysema.

Committee Discussion: *The committee acknowledged that there is no data on safety and feasibility of coil removal.*

5. **DISCUSSION:** Future Post-Market Study

Should the device be found approvable, please comment on whether a post-approval study would be recommended, and if so:

a. Please comment on which safety and effectiveness endpoints should be collected.
b. Please comment whether a registry would be an appropriate mechanism to collect the desired information.

Committee Discussion: *The committee acknowledged the benefit of a registry. The committee stated to consider other primary endpoints such as PFTs, 6MWT or BODE index. They also suggested monitoring hospitalization, ER visits, any hemoptysis, pneumonia, CT imaging to follow up and monitor fibrotic response.*

6. VOTE: Based on data in the briefing materials and presentations at today's meeting, do you believe the **ELEVAIR™ Endobronchial Coil System** is safe for use in patients who meet the criteria specified in the proposed indication; while considering the additional procedures needed to maintain effectiveness?

Vote Result: Yes: **7** No: **5** Abstain: **0**

7. **VOTE:** Based on data in the briefing materials and presentations at today's meeting, do you Believe there reasonable assurance that the **ELEVAIR™ Endobronchial Coil System** is effective for use in patients who meet the criteria specified in the proposed indication?

Vote Result: Yes: **5** No: **7** Abstain: **0**

8. **VOTE:** Based on data in the briefing materials and presentations at today's meeting, do you believe the benefits of the **ELEVAIR™ Endobronchial Coil System** outweigh the risks for use in patients who meet the criteria specified in the proposed indication?

Vote Result: Yes: **3** No: **8** Abstain: **1**

Please see the transcript for details of the committee's discussions.

The meeting was adjourned at approximately 6:00 p.m.

I certify that I attended the PneumRx, Inc.'s ELEVAIR™ Endobronchial Coil System meeting of the Anesthesiology and Respiratory Therapy Devices Panel of the Medical Devices Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

Evella F. Washington

Evella Washington
Designated Federal Officer