Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Oncologic Drugs Advisory Committee
September 14, 2016

Location: Tommy Douglas Conference Center
10000 New Hampshire Avenue, Silver Spring, Maryland 20903

Topic: The committee met to discuss new drug application 208714, apaziquone for intravesical instillation, application submitted by Spectrum Pharmaceuticals, Inc. The proposed indication (use) for this product is for immediate intravesical instillation post-transurethral resection of bladder tumors in patients with non-muscle invasive bladder cancer.

These summary minutes for the September 14, 2016, meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on October 14, 2016.

I certify that I attended the September 14, 2016, meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/
Lauren D. Tesh, PharmD, BCPS
Designated Federal Officer, ODAC

/S/
Bruce J. Roth, MD
Chairperson, ODAC

Oncologic Drugs Advisory Committee Meeting
September 14, 2016

The following is the final report of the Oncologic Drugs Advisory Committee (ODAC) meeting held on September 14, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Office of Hematology and Oncology Products and posted on the FDA website at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/ucm486395.htm

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

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on September 14, 2016, at the Tommy Douglas Conference Center, 10000 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the briefing materials from the FDA and Spectrum Pharmaceuticals, Inc. The meeting was called to order by Bruce J. Roth, MD (Chairperson); the conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 80 people in attendance. There were five (5) Open Public Hearing speakers.

Issue: The committee discussed new drug application 208714, apaziquone for intravesical instillation, application submitted by Spectrum Pharmaceuticals, Inc. The proposed indication (use) for this product is for immediate intravesical instillation post-transurethral resection of bladder tumors in patients with non-muscle invasive bladder cancer.

Attendance:
ODAC Members Present (Voting): Bernard F. Cole, PhD; Grzegorz S. Nowakowski, MD; Vassiliki Papadimitrakopoulou, MD; Gregory J. Riely, MD, PhD; Brian I. Rini, MD, FACP; Bruce J. Roth, MD (Chairperson); Thomas S. Uldrick, MD, MS

ODAC Members Present (Non-Voting): Phuong Khanh (P.K.) Morrow, MD, FACP (Industry Representative)

ODAC Members Not Present (Voting): Harold J. Burstein, MD, PhD; Heidi D. Klepin, MD, MS; Jeffrey E. Lancet, MD; Albert S. Pappo, MD; Courtney J. Preusse, MA (Consumer Representative); Alice T. Shaw, MD, PhD

Temporary Members (Voting): Karim Chamie, MD, MSHS; Mark L. Gonzalgo, MD, PhD; Pamela J. Haylock, PhD, RN (Acting Consumer Representative); Brent Logan, PhD; Patricia A. Spears (Patient Representative); Jennifer M. Taylor, MD, MPH; John A. Taylor, III, MD, MS

FDA Participants (**Non-Voting):** Richard Pazdur, MD; Geoffrey Kim, MD; V. Ellen Maher, MD; Gwynn Ison, MD; Chana Weinstock, MD; Erik Bloomquist, PhD

Designated Federal Officer (Non-Voting): Lauren D. Tesh, PharmD, BCPS

Open Public Hearing Speakers: Mark Krivel; Ed Silver; Andrea Maddox-Smith (The Bladder Cancer Advocacy Network); Michaela O'Hearn; Raoul S. Concepcion, MD, FACS (Vanderbilt University School of Medicine and The Comprehensive Prostate Center)

The agenda proceeded as follows:

Call to Order and Introduction of Committee	**Bruce J. Roth, MD** Chairperson, ODAC
Conflict of Interest Statement	**Lauren Tesh, PharmD, BCPS** Designated Federal Officer, ODAC
Opening Remarks	**Chana Weinstock, MD** Medical Officer, Genitourinary Cancers Team Division of Oncology Products 1 (DOP1) Office of Hematology & Oncology Products (OHOP) Office of New Drugs (OND), CDER, FDA
GUEST SPEAKER PRESENTATION	
Overview of Diagnosis and Management of Non-Muscle Invasive Bladder Cancer	**Seth P. Lerner, MD, FACS** Professor, Scott Department of Urology Beth and Dave Swalm Chair in Urologic Oncology Director of Urologic Oncology Director of the Multidisciplinary Bladder Cancer Program Baylor College of Medicine Medical Center Houston, Texas
APPLICANT PRESENTATIONS	**Spectrum Pharmaceuticals, Inc.**
Introduction	**Anil K. Hiteshi, RAC** Global Regulatory Affairs Spectrum Pharmaceuticals, Inc.
Post-Operative Intravesical Therapy	**Neal Shore, MD** Medical Director Carolina Urologic Research Center

APPLICANT PRESENTATIONS (CONT.)

Clinical Efficacy and Safety	**Gajanan Bhat, PhD** Vice President, Biostatistics, Data Management and Medical Writing Spectrum Pharmaceuticals, Inc.
Benefit-Risk and Clinical Utility of Apaziquone	**Alfred Witjes, MD** Professor of Urologic Oncology Radbound University Nijmegen Medical Centre
Clinical Perspective	**Mark Soloway, MD** Chief of Urological Oncology Memorial Cancer Institute, Miami
Concluding Remarks	**Rajesh Shrotriya, MD** Chairman and Chief Executive Officer Spectrum Pharmaceuticals, Inc.

FDA PRESENTATIONS

NDA 208714 - Apaziquone	**Gwynn Ison, MD** Medical Officer DOP1, OHOP, OND, CDER, FDA
FDA Statistical Analysis	**Erik Bloomquist, PhD** Statistical Reviewer Division of Biometrics V (DBV) Office of Biometrics (OB) Office of Translational Sciences (OTS) CDER, FDA

Clarifying Questions to the Presenters

BREAK

Open Public Hearing

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **VOTE:** Has substantial evidence of a treatment effect for apaziquone over placebo been demonstrated?

   Voting Results YES: 0 NO: 14 ABSTAIN: 0

   Committee Discussion:

   The committee noted that this drug may have activity in patients with NMIBC but based on the data that was presented, it was unanimously agreed that substantial evidence of efficacy had not been shown. One statistician on the panel stated that the sponsor did not meet their primary endpoints in both studies, 611 and 612, and that the subgroup analyses were ad-hoc and could lead to potentially biased estimates of the treatment effect in the subgroups of interest. In addition, it was commented that the pooled analysis of the two studies didn't have a prospective protocol. The pooled analysis of 611 and 612 was done post-hoc and doesn't provide the same level of statistical certainty or robustness as the two separate trials would have. Also, the committee noted there was a substantial amount of missing data and that this may have impacted the estimated effect. The committee recommended that the sponsor continue the development of this drug because of the unmet need in this population and the seemingly low toxicity profile of apaziquone compared to current therapy. One committee member noted that to encourage development in nonmuscle-invasive bladder cancer that the urologic community needs to further define appropriate endpoints for clinical trials. Please see the transcript for details of the committee discussion.

2. **DISCUSSION:** For those who voted "yes" to question 1 that an effect has been demonstrated, please discuss the clinical meaning of the results of studies 611 and 612.

   Committee Discussion: *The unanimous vote of NO to question 1 precluded the need for this discussion. Please see the transcript for details of the committee discussion.*

   The meeting was adjourned at approximately 11:57 a.m.