Duke UNIVERSITY | Duke-Margolis Center *for* Health Policy

Advancing Drug Development for the Prevention and Treatment of Respiratory Syncytial Virus Infections

Marriott Marquis ● Washington, DC
May 2, 2016

Meeting objectives: The objectives for this event are to: 1) explore possible definitions for respiratory syncytial virus (RSV) disease severity; 2) identify and discuss populations that will be evaluated in clinical trials; 3) identify and discuss clinically meaningful endpoints to be used to assess efficacy of drugs designed for prevention and to treat illness due to RSV; 4) describe nonclinical and clinical approaches to developing products that will be primarily used in the pediatric population; 5) explore the types of proof-of-concept data needed to initiate clinical trials in infants and young children; and 6) discuss RSV drug development for other populations, such as elderly and immunocompromised patients.

9:00 a.m. **Welcome, Overview, and Meeting Objectives**
Greg Daniel, Duke-Margolis Center for Health Policy

9:15 a.m. **Opening Remarks**
Jeff Murray, US Food and Drug Administration

9:30 a.m. **Facilitating Drug Development for Treatment of Respiratory Syncytial Virus (RSV) Infections**
Alan Shapiro, US Food and Drug Administration

9:45 a.m. **Session I: Issues Related to RSV Bronchiolitis Treatment Trials Establishing Definitions and Identifying Endpoints**

Session 1a: Establishing Definitions of At-Risk Populations and Disease Severity
Moderator: Greg Daniel, Duke-Margolis Center for Health Policy

Opening Presentation: Robert Welliver, University of Oklahoma Health Sciences Center

- How do we define disease severity in the population to be studied (e.g., "moderate" disease, "severe" disease, or all symptomatic illness)?
- What other factors are important in defining the study population (e.g., chronological age, underlying risk factors for severe illness, upper versus lower respiratory tract illness)?

Discussion *(30 minutes)*

10:30 a.m. **Break**

10:45 a.m. **Session Ib: Identifying Appropriate Endpoints for RSV Bronchiolitis Treatment Trials**

Moderator: Greg Daniel, Duke-Margolis Center for Health Policy

Opening Presentation: Cody Meissner, Tufts University School of Medicine (*10 min*)

Panelists:

- Selena Daniels, U.S. Food and Drug Administration (*5-7 min*)
- Jason Chien, Gilead Sciences (*5-7 min*)
- Barbara Rath, International Society for Influenza and Other Infectious Diseases (*5-7 min*)
- Flor Munoz, American Academy of Pediatrics (*5-7 min*)

Questions to address:

- Which signs and symptoms should be included in an instrument used to capture clinical severity of RSV?
- What should the primary outcome measurement be to establish treatment efficacy? Time to reach a pre-determined score? Change in score on a pre-determined day of illness? Other possibilities?
- Can the same signs and symptoms (or the same instrument) be used for study inclusion criteria and for establishing treatment response?
- Are two symptom instruments needed to measure treatment response: one for clinicians and one for caregivers? How would they be combined in an endpoint?
- Is there support among the pediatric and infectious disease community for validating a clinical tool to measure disease severity for RSV illness among infants (e.g., < 12 months of age)?
- Are there potential secondary endpoints that might be considered clinically meaningful and supportive (e.g., RSV viral load, biomarkers)?

Discussion *(65-75 minutes)*

12:30 p.m. **Lunch**

1:30 p.m. **Session II: Identifying Alternative Endpoints for Prevention of RSV Bronchiolitis**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Opening Presentation: Jeff Roberts, US Food and Drug Administration (*15 min*)

Questions to be addressed:

- Should a novel prophylaxis product prevent all symptomatic RSV-related illness or only the most severe manifestations? What degree of illness-reduction is clinically meaningful?
- Given the differences in natural history of the illness in different populations, are different endpoints needed for different populations (i.e. healthy infants, premature infants, or those with underlying conditions)?
- The pivotal studies supporting approval of palivizumab employed hospitalization as the primary endpoint, which may no longer be the ideal endpoint, making a non-inferiority margin based on previous palivizumab trials difficult to justify. What is the best way to assess novel prophylaxis products in the context of the approved product?

- To what extent can prophylaxis efficacy from one group of infants be extrapolated to another? For example, can efficacy in healthy full-term infants be extrapolated to infants at higher risk of severe illness (e.g. prematurity, chronic lung disease, congenital heart disease)?

Discussion *(30-45 minutes)*

2:30 p.m. **Session III: Initiation of Pediatric Trials for RSV Bronchiolitis**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Opening Presentation: Prabha Viswanathan, US Food and Drug Administration

Questions to be addressed:

- What types of proof-of-concept studies are needed to support initiation of pediatric studies for treatment and prevention products?
    - Which adult populations/disease conditions are preferred?
    - To what extent can non-clinical data be used to support pediatric studies (i.e., animal models of disease)?
    - Are adult challenge studies adequate to demonstrate proof-of-concept for infant bronchiolitis trials?

Discussion *(30 minutes)*

3:15 p.m. Break

3:30 p.m. **Session IV: Encouraging RSV Drug Development in Other Populations**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Panelists:

- Filip Dubovsky, MedImmune/AstraZeneca (*5-7 min*)
- Edward Walsh, University of Rochester (*5-7 min*)
- Michael Boeckh, Fred Hutchinson Cancer Research Center (*5-7 min*)

Questions to be addressed:

- How do we encourage RSV drug development in other populations such as elderly or immunocompromised patients?
    - What are the unique considerations for trials in older children and adults? Are different endpoints required?
    - What is the optimal approach to studying small populations such as stem cell transplant populations, in which the sample size may be small and controlled trials are difficult to conduct?
    - Should both prophylaxis and treatment be evaluated in non-pediatric populations?

Discussion *(25-30 minutes)*

4:15 p.m. **Identifying Next Steps**
Mark McClellan, Duke-Margolis Center for Health Policy

4:30 p.m. **Closing Remarks**
Mark McClellan, Duke-Margolis Center for Health Policy

4:45 p.m. **Adjournment**

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