Public Workshop
Developing Antibacterial Drugs That Target a Single Species

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OND/CDER/OMPT/FDA

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Welcome

Public Workshop — Developing Antibacterial Drugs That Target a Single Species

• An opportunity for discussion
• Not an Advisory Committee
• Conflict of interest disclosures available
• Open time for public comment
Panel Introductions
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<td>Introduction</td>
<td>Ed Cox</td>
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<td>8:45-9:00</td>
<td>Overview of Case Study</td>
<td>Peter Kim</td>
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<td>9:00-10:30</td>
<td>Perspectives on the case</td>
<td>Helen Boucher</td>
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<td>Industry</td>
<td>John Tomayko</td>
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<td>EMA</td>
<td>Marco Cavaleri</td>
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<td>10:30-10:45</td>
<td>Break</td>
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<td>10:45-11:15</td>
<td>Clarifying Questions (Panelists and Audience)</td>
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<td>11:15-12:15</td>
<td>Presentation of the Clinical program</td>
<td>John Rex</td>
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<td>12:15-1:00</td>
<td>Lunch</td>
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<td>1:00-1:30</td>
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<td>1:30-2:00</td>
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<td>2:00-3:45</td>
<td>Panel Discussion</td>
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<td>Next steps/concluding remarks</td>
<td>Ed Cox</td>
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Developing Drugs Targeting a Single Species

• Can do if species occurs with at least a moderate degree of frequency
  – skin infections caused by *S. aureus*

• Challenging if species of interest occurs infrequently
  – Number of patients needed using usual statistical conventions for an infrequently occurring species exceeds what likely can be achieved in relevant time frames

• Rapid diagnostics very important
  – can help guide clinical use of such a species specific therapy and support prudent use
  – can help, but won’t solve the challenges of clinical trials for infrequently occurring species
Drugs Targeting a Single Species

• Some investigational agents target a single species that causes disease infrequently
• Drugs active against only a single species should have less of an effect on normal flora
  – will they promote resistance less than broader agents?
  – less alteration of normal flora and less shifting of flora to more resistant bacteria and fungal colonization that may lead to infection?
  – will we see less *C. diff* colitis?
• What would the clinical role be for such a drug?
Disease Characteristics and Trial Designs

- Serious acute bacterial diseases
- Oncologic conditions
- HIV/HCV
- Rare metabolic disorders
  - Identifying patients
  - Disease course over time
  - Diagnostic certainty
  - Urgency to initiate therapy
  - Variability in outcomes and time to clinical outcome
  - Opportunities for rescue therapy for patient not responding
What to Do When Species of Interest is Infrequent?

• Less precise estimates of efficacy / greater uncertainty
• May not achieve usual statistical conventions
• Particularly challenging where outcomes for serious acute bacterial disease are variable depending on factors known and unknown
• Effects are not “lights on vs. lights off” e.g., a shift from 90% to 10%
Evaluating Efficacy

- Options for discussion include:
  - accepting greater uncertainty from clinical data?
    - small numbers of patients
    - concomitant therapy
  - if clinical trials not feasible / practical
    - animal rule to evaluate efficacy?
    - safety data from humans
    - provisions for restrictions on conditions of availability
  - other ideas?
Animal Models for Evaluating Efficacy Under the Animal Rule

- Predictive of response in humans – not just to measure activity
- Is there a “good animal model of infection”
- Lots of difficult questions
  - which species?
    - similar or different susceptibility
  - what inoculum?
  - when to intervene with test drug?
  - animal may metabolize/clear drug differently
Discussion

• Pros and Cons of different potential pathways for development
  – Clinical data
  – Animal data

• Important to have a pathway for development so that the potential for such drugs for treating patients can be evaluated
• Thank you