Review of Antibiotics in Clinical Development Pipeline

Wes Kim
Senior Officer, Antibiotic Resistance Project
The Pew Charitable Trusts

Enhancing the Clinical Trial Enterprise for Antibacterial Drug Development in the United States. November 18-19, 2019
Summary of 2014 – 2018 antibiotics pipeline longitudinal analysis

- **20** New Entrants
- **67** Total Drugs In Clinical Development
- **10** Approved
- **10** Stalled
- **15** Discontinued
Most of the candidates are based on previously discovered classes.

Total Number of Drug Candidates from 2014 - 2018: 67

**Gram-Negative**
- Novel Class: 4
- Prior Class: 22
  - In Development: 3
  - Discontinued / Stalled: 1
  - Approvals: 2

**Gram-Positive**
- Novel Class: 13
- Prior Class: 28
  - In Development: 5
  - Discontinued / Stalled: 8
  - Approvals: 4

Most of the candidates are based on previously discovered classes.
# Antibiotic approvals: 2014 - 2019

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
<th>Approved</th>
<th>Novel</th>
<th>Activity Against Gram-Negative ESKAPE?</th>
<th>Indicated for WHO Critical Pathogen?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalvance (dalbavancin)</td>
<td>Durata Therapeutics Inc.</td>
<td>2014</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Orbactiv (oritavancin)</td>
<td>The Medicines Company</td>
<td>2014</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Sivextro (tedizolid)</td>
<td>Cubist Pharmaceuticals Inc.</td>
<td>2014</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Zerbaxa (ceftolozane + tazobactam)</td>
<td>Cubist Pharmaceuticals Inc.</td>
<td>2014</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Avycaz (ceftazidime + avibactam)</td>
<td>AstraZeneca plc/ Actavis plc</td>
<td>2015</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Baxdela (delafloxacin)</td>
<td>Melinta Therapeutics, Inc.</td>
<td>2017</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Vabomere (meropenem + vaborbactam)</td>
<td>The Medicines Company</td>
<td>2017</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Zemdri (plazomicin)</td>
<td>Achaogen, Inc.</td>
<td>2018</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Nuzyra (omadacycline)</td>
<td>Paratek Pharmaceuticals, Inc.</td>
<td>2018</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Xerava (eravacycline)</td>
<td>Tetraphase Pharmaceuticals, Inc.</td>
<td>2018</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Recarbrio (imipenem/cilastatin + relebactam)</td>
<td>Merck &amp; Co., Inc.</td>
<td>2019</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Xenleta (lefamulin)</td>
<td>Nabriva Therapeutics</td>
<td>2019</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Fetroja (Cefiderocol)</td>
<td>Shionogi &amp; Co., Ltd.</td>
<td>2019</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
</tbody>
</table>
Recent pipeline analysis demonstrates continued insufficient candidates in development

As of June 30, 2019...

• 42 (small molecule) antibiotics in clinical development
• No new entrants
• Year-over-year, total number of candidates have been steady

Also, four NDA’s under review and one complete response. (Since then, three approvals and one company seeking development partner).

Of the 13 candidates in Ph 3...
• **Three** are based on novel classes (but one has now been discontinued)
• **Six** have expected activity against a CDC ‘Urgent’ threat (CRE, CRAB, C. difficile, drug-resistant gonorrhoeae)
Recent pipeline analysis demonstrates continued insufficient candidates in development

- At least 17 of the 42 antibiotics in development have the potential to treat infections caused by Gram-negative ESKAPE pathogens—a critical area of unmet need.
- But, only 1 of these 17 represents a novel class (and Ph 3 studies have since been terminated)
How to reinvigorate the antibiotics pipeline?

• How do we populate the pipeline with more differentiated antibiotics?
• Other than financial push and pull incentives, what other levers are available?
Acknowledgements

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Thank you