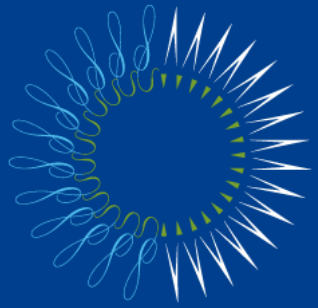

THE PEW CHARITABLE TRUSTS

Review of Antibiotics in Clinical Development Pipeline

Wes Kim
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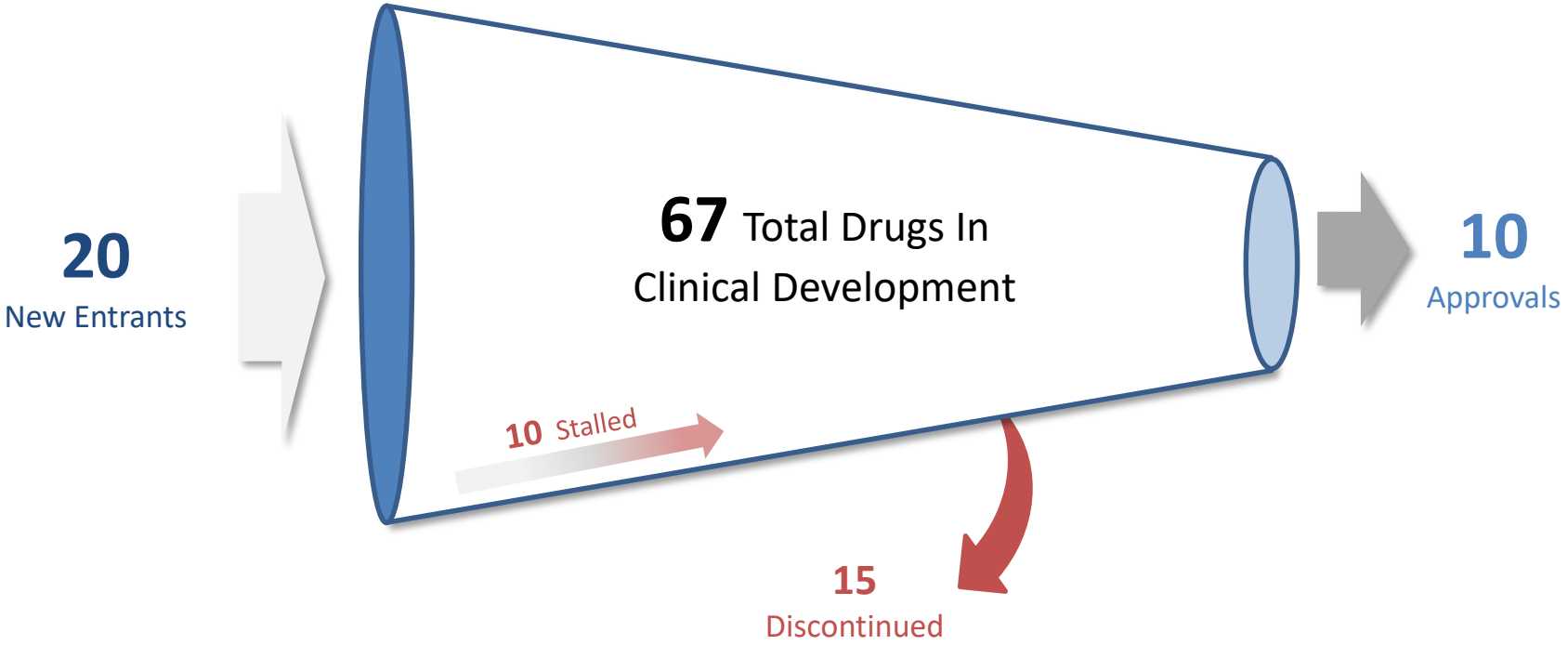
The Pew Charitable Trusts

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



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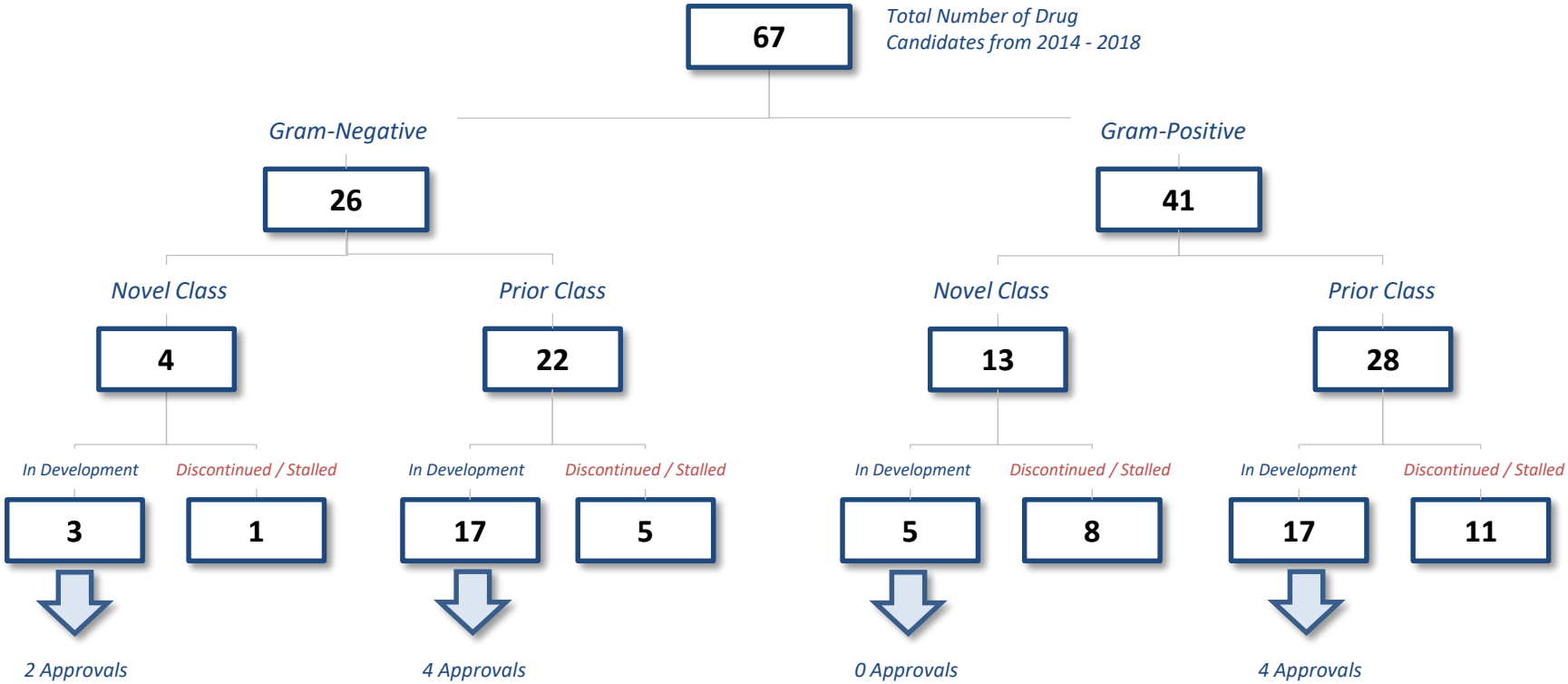
Most of the candidates are based on previously discovered classes



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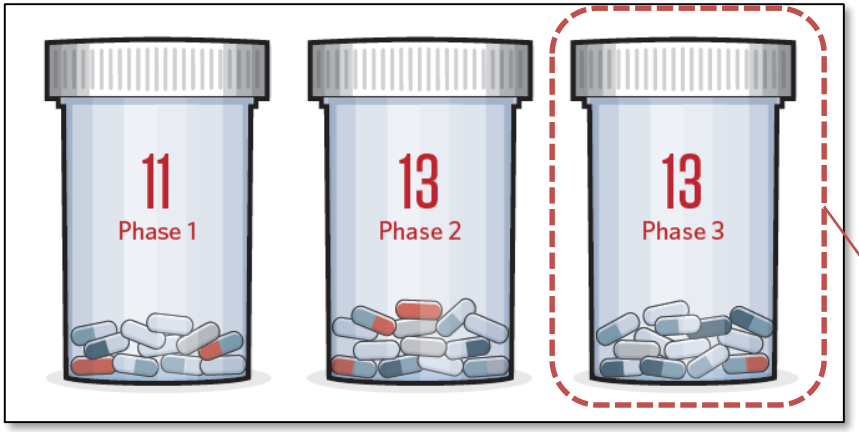
Antibiotic approvals: 2014 - 2019

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

Recent pipeline analysis demonstrates continued insufficient candidates in development

As of June 30, 2019…



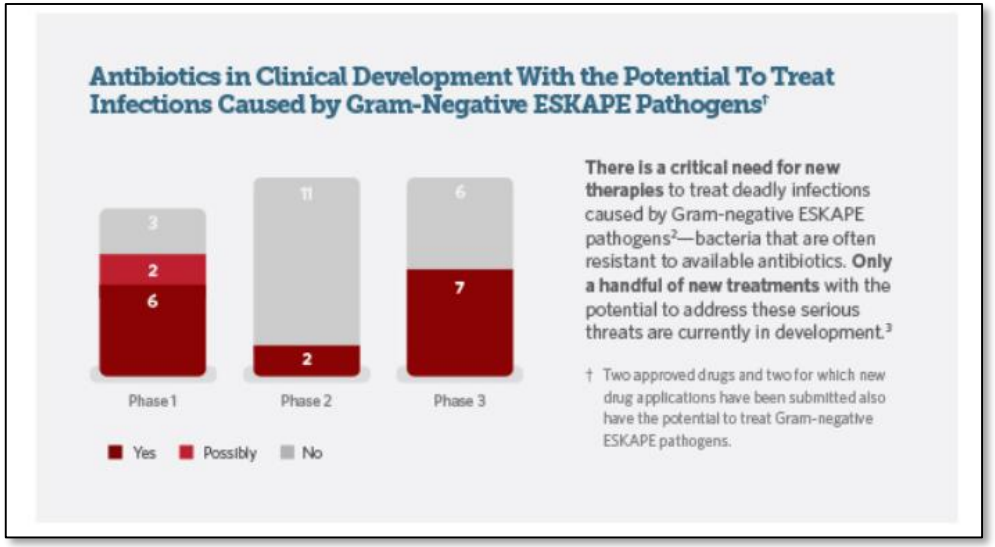
Also, four NDA's under review and one complete response. (Since then, three approvals and one company seeking development partner).

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

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)**

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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?

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Acknowledgements

- Cara Lepore (Pew)

- Lloyd Czaplewski
- Lynn Silver
- Ursula Theuretzbacher

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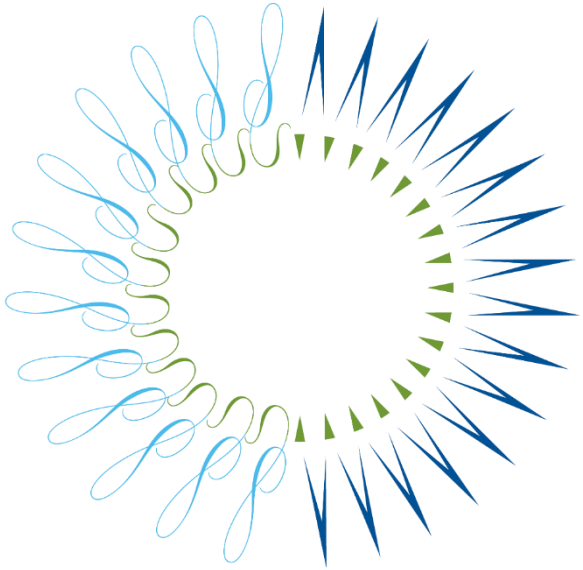
Thank you



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