Antibiotics Currently in Clinical Development

Note: This data visualization was updated in May 2017 with new data.

As of March 2017, approximately 41 new antibiotics[1] with the potential to treat serious bacterial infections are in clinical development for the U.S. market. The success rate for clinical drug development is low; historical data show that, generally, only 1 in 5 infectious disease products that enter human testing (phase 1 clinical trials) will be approved for patients.* Below is a snapshot of the current antibiotic pipeline, based on publicly available information and informed by an external expert. It will be updated periodically, as products advance or are known to drop out of development. Because this list is updated periodically, footnote numbers may not be sequential. Please contact **abxpipeline@pewtrusts.org** with additions or updates.

Drug name	Company	Drug class	Target	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
New Drug Application (NDA) submitted[2]						
Baxdela (delafloxacin)	Melinta Therapeutics Inc.	Fluoroquinolone	Bacterial type II topoisomerase	Possibly	Possibly	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia,** complicated urinary tract infections[6]
Meropenem + Vaborbactam	Rempex Pharmaceuticals Inc. (wholly owned subsidiary of The Medicines Co.)	β-lactam (carbapenem) + β-lactamase inhibitor (cyclic boronate)[16,18]	PBP; β-lactamase	Yes	Yes	**Complicated urinary tract infections, complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia, febrile neutropenia,** bacteremia, acute pyelone-phritis (some indications specifically target infections caused by carbapenem-resistant Enterobacteriaceae)
Phase 1[2]						
CRS3123	Crestone Inc.	Diaryldiamine[16]	Methionyl-tRNA synthetase[17]	No	Yes	*C. difficile* infections
ETX2514SUL[10]	Entasis Therapeutics Inc.	β-lactam (sulbactam) + β-lactamase inhibitor (diazabicyclooctane)	PBP; β-lactamase	Yes	No	Bacterial infections (caused by *Acinetobacter baumannii*)[6]
GSK-3342830[10]	GlaxoSmithKline PLC (Shionogi licensee)	β-lactam (cephalosporin)	PBP	Possibly	Possibly	Bacterial infections

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Drug name	Company	Drug class	Target	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Phase 1[2] (continued)						
KBP-7072	KBP BioSciences Pharmaceutical Technical Co. Ltd.	Tetracycline	30S subunit of bacterial ribosome	Possibly	No	**Community-acquired bacterial pneumonia**[6]
LCB01-0371[10]	LegoChem Biosciences Inc.	Oxazolidinone	50S subunit of bacterial ribosome	No	No	Bacterial infections
MCB3837	Morphochem AG	Oxazolidinone-quinolone hybrid	50S subunit of bacterial ribosome; bacterial type II topoisomerase	No	Yes	*C. difficile* **infections**[6]
MGB-BP-3[10]	MGB Biopharma Ltd.	Distamycin[16]	DNA minor groove[17]	No	Yes	*C. difficile*-**associated diarrhea**
Nacubactam (OP0595/ RG6080)[10]	Meiji Seika Pharma Co. Ltd./Fedora Pharmaceuticals Inc. (Roche licensee)	β-lactamase inhibitor (diazabicyclooctane)	β-lactamase, PBP2	Possibly	Possibly	Bacterial infections
SPR741[6,10,19]	Spero Therapeutics	Polymyxin	Cell membrane[17]	Possibly	Possibly	Bacterial infections
TD-1607	Theravance Biopharma Inc.	Glycopeptide-β-lactam (cephalosporin) hybrid	PG chain elongation; PBP	No	No	**Acute bacterial skin and skin structure infections,**[6] **hospital-acquired pneumonia/ventilator-associated bacterial pneumonia,**[6] **bacteremia**[6]
TP-271	Tetraphase Pharmaceuticals Inc.	Tetracycline	30S subunit of bacterial ribosome	Possibly	Possibly	**Community-acquired bacterial pneumonia**
TP-6076[6]	Tetraphase Pharmaceuticals Inc.	Tetracycline	30S subunit of bacterial ribosome	Possibly	Possibly	Bacterial infections
WCK 2349	Wockhardt Ltd.	Fluoroquinolone (WCK 771 pro-drug)	Bacterial type II topoisomerase	No	No	**Hospital-acquired bacterial pneumonia**[6]
WCK 771	Wockhardt Ltd.	Fluoroquinolone	Bacterial type II topoisomerase	No	No	**Hospital-acquired bacterial pneumonia**[6]

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Drug name	Company	Drug class	Target	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Phase 1[2] (continued)						
Cefepime + Zidebactam (WCK 5222)	Wockhardt Ltd.	β-lactam (cephalosporin) + β-lactamase inhibitor (diazabicyclooctane)	PBP; β-lactamase	Yes	Possibly	**Complicated urinary tract infections,**[6] **hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia**[6]
Phase 2[2]						
Aztreonam + Avibactam[7,10] (ATM-AVI)	Pfizer Inc./Allergan PLC (formerly Actavis)	β-lactam (monobactam) + β-lactamase inhibitor (diazabicyclooctane)	PBP; β-lactamase	Yes	Yes	Complicated intra-abdominal infections
Brilacidin	Cellceutix Corp.	Defensin mimetic[16]	Cell membrane	No	No	**Acute bacterial skin and skin structure infections**
CG400549	CrystalGenomics Inc.	Benzyl pyridinone[16]	FabI[17]	No	No	Acute bacterial skin and skin structure infections, osteomyelitis[6]
Afabicin (Debio 1450)	Debiopharm International SA	Benzofuran naphthyridine[16]	FabI[17]	No	No	**Acute bacterial skin and skin structure infections and osteomyelitis (*Staphylococcus*-specific)**
Finafloxacin[11,12]	MerLion Pharmaceuticals Pte Ltd.	Fluoroquinolone	Bacterial type II topoisomerase	Yes[13]	Possibly	**Complicated urinary tract infections, acute pyelonephritis (kidney infection), complicated intra-abdominal infections, acute bacterial skin and skin structure infections**
Gepotidacin (GSK2140944)[15]	GlaxoSmithKline PLC	Triazaacenaphthylene[16]	Bacterial type II topoisomerase (novel A subunit site)[17]	No	Yes	Complicated urinary tract infections,[6] **uncomplicated urinary tract infections**, acute bacterial skin and skin structure infections, **uncomplicated urogenital gonorrhea**, and community-acquired bacterial pneumonia[6]
MRX-I[14]	MicuRx Pharmaceuticals Inc.	Oxazolidinone	50S subunit of bacterial ribosome	No	No	Acute bacterial skin and skin structure infections
Nafithromycin (WCK 4873)	Wockhardt Ltd.	Macrolide	50S subunit of bacterial ribosome	No	No	**Community-acquired bacterial pneumonia**
Nemonoxacin[8]	TaiGen Biotechnology Co. Ltd.	Quinolone	Bacterial type II topoisomerase	No	No	**Community-acquired bacterial pneumonia,** diabetic foot infection, **acute bacterial skin and skin structure infections**
Murepavadin (POL7080)[10]	Polyphor Ltd.	Antimicrobial peptide mimetic[16]	LptD[17]	Yes (*Pseudomonas*)	No	**Ventilator-associated bacterial pneumonia** (caused by *Pseudomonas aeruginosa*), lower respiratory tract infection, bronchiectasis

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Drug name	Company	Drug class	Target	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Ramoplanin	Nanotherapeutics Inc.	Lipodepsipeptide[16]	Lipid I,II	No	Yes	Prevention of recurrent *C. difficile* infection[6]
Ridinilazole (SMT 19969)	Summit Therapeutics Inc.	Bis-benzimidazole[16]	Unknown	No	Yes	***C. difficile* infection**
Zoliflodacin (ETX0914)	Entasis Therapeutics Inc.	Spiropyrimidenetrione[16]	Bacterial type II topoisomerase (GyrB)[17]	No	Yes	**Uncomplicated gonorrhea**
Phase 3[2]						
Cadazolid	Actelion Pharmaceuticals Ltd.	Oxazolidinone-quinolone hybrid	50S subunit of bacterial ribosome; bacterial type II topoisomerase	No	Yes	***C. difficile* infection**
Cefiderocol (S-649266)[15]	Shionogi & Co. Ltd.	Siderophore-β-lactam (cephalosporin)	PBP	Yes	Yes	**Complicated urinary tract infections, carbapenem-resistant Gram-negative bacterial infections**
Eravacycline	Tetraphase Pharmaceuticals Inc.	Tetracycline	30S subunit of bacterial ribosome	Yes	Yes	**Complicated intra-abdominal infections, complicated urinary tract infections**
Iclaprim	Motif Bio PLC	2,4-diaminopyrimidine	Dihydrofolate reductase	No	No	**Acute bacterial skin and skin structure infections; hospital-acquired bacterial pneumonia**
Imipenem/ cilastatin + relebactam (MK-7655)	Merck & Co. Inc.	β-lactam (carbapenem) + β-lactamase inhibitor (diazabicyclooctane)	PBP; β-lactamase	Yes	Yes	**Complicated urinary tract infections,** acute pyelonephritis, **complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia**
Lefamulin (BC-3781)	Nabriva Therapeutics AG	Pleuromutilin[16]	50S subunit of bacterial ribosome	No	No	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia,** hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia,[6] osteomyelitis,[6] prosthetic joint infections[6]
Omadacycline	Paratek Pharmaceuticals Inc.	Tetracycline	30S subunit of bacterial ribosome	Yes	Possibly	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections, complicated urinary tract infections**

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Drug name	Company	Drug class	Target	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Phase 3[2] (continued)						
Plazomicin	Achaogen Inc.	Aminoglycoside	30S subunit of bacterial ribosome	Yes	Yes	**Complicated urinary tract infections** including acute pyelonephritis, **catheter-related bloodstream infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia, complicated intra-abdominal infections** in patients with limited treatment options (some indications specifically target infections caused by carbapenem-resistant Enterobacteriaceae)
Solithera (Solithromycin)	Cempra Inc.	Macrolide	50S subunit of bacterial ribosome	No	Yes	**Community-acquired bacterial pneumonia, uncomplicated urogenital gonorrhea**, urethritis[6]
Taksta (fusidic acid)[9]	Cempra Inc.	Fusidane	Elongation factor G	No	No	Prosthetic joint infections, **acute bacterial skin and skin structure infections**
Zabofloxacin[6]	Dong Wha Pharmaceutical Co. Ltd	Fluoroquinolone	Bacterial type II topoisomerase	No	No	Community-acquired bacterial pneumonia

For definitions of drug development terms, visit:

http://www.pewtrusts.org/en/research-and-analysis/analysis/2014/03/12/glossary-for-the-antibiotic-pipeline

Note: The following drugs have been removed from the pipeline. They will be included in future updates if development resumes:

March 2017 review: Ceftaroline + Avibactam was removed during the March 2017 review because it was no longer included in the research and development pipelines on the company's website.

September 2016 review: BAL30072 (Basilea Pharmaceutica Ltd.) was removed during the September 2016 review because it was no longer included in the research and development pipeline on the company website.

March 2016 review: Radezolid, Debio 1452, avarofloxacin, and surotomycin were removed during the March 2016 review. Radezolid was removed because systemic indications for this product were no longer included in the development plans listed on the sponsor website. Debio 1452, avarofloxacin, and surotomycin were no longer included in the research and development pipelines on the company website.

September 2015 review: No changes.

March 2015 review: No changes.

December 2014 review: EDP-788 (Enanta Pharmaceuticals) and TD-1792 (Theravance Biopharma) were removed during the December 2014 review. These drugs were either no longer included in the research and development pipelines on the company website, or there was direct communication from the company regarding the status of the drugs. Additionally, GSK-2696266, which had been removed during the September 2014 review, is included in this pipeline again as S-649266, which is being developed by Shionogi.

September 2014 review: GSK-2696266 and GSK-1322322 (GlaxoSmithKline), ACHN-975 (Achaogen), and LFF571 (Novartis) were removed during the September 2014 review. These drugs were either no longer included in the research and development pipelines on the company website, or there was direct communication from the company regarding the status of the drugs.

June 2014 review: Ceftobiprole, an antibiotic developed by Basilea Pharmaceutica, had been included in our analysis; however, the company announced in June 2014 that it is not pursuing further development in the United States until a partner has been acquired. (As of April 2016, Basilea announced a partnership with BARDA for phase 3 development of ceftobiprole in the United States. This product will be included in our pipeline once development commences.)

* Michael Hay et al., "Clinical Development Success Rates for Investigational Drugs," *Nature Biotechnology* 32, no. 1 (2014): 40–51, doi:10.1038/nbt.2786. See more at http://www.pewtrusts.org/en/multimedia/data-visualizations/2014/antibiotics-currently-in-clinical-development.

Endnotes

1 Antibiotics listed here include products containing at least one component not approved in the United States previously. All analyses were strictly limited to systemic antibiotics (drugs that work throughout the body) and drugs to treat *Clostridium difficile*-associated disease. The Centers for Disease Control and Prevention cited *C. difficile* as an urgent public health threat in a 2013 report (*Antibiotic Resistance Threats in the United States, 2013* (2013), http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf). This pipeline is also limited to drugs with the potential to treat serious or life-threatening infections. Specifically excluded were drugs to treat mycobacterial infections, such as tuberculosis and *Mycobacterium avium* complex, *Helicobacter pylori,* and biothreat pathogens. Additionally, biological products, vaccines, and locally acting drugs such as topical, ophthalmic, and inhaled products were excluded. Avibactam, a novel beta-lactamase inhibitor, is being studied in combination with three approved antibiotics, and all three were counted for this report as each combination targets a distinct set of pathogens.

2 Based on the most advanced development phase for any indication according to trials registered in clinicaltrials.gov, unless direct communication from the company indicated differently. If no trials were included in clinicaltrials.gov, then the phase listed on the company website or provided directly by the company is noted. Antibiotics that have been approved will remain listed for one year following approval of the initial indication.

3 A 'yes' in this column indicates that a drug has in vitro data showing both activity against one or more Gram-negative species that are considered ESKAPE pathogens (*Klebsiella pneumoniae*, *Acinetobacter baumanii*, or *Pseudomonas aeruginosa,* and *Enterobacter* species) and the potential for clinically significant improved coverage of resistant isolates of these species relative to currently available antibiotics. Excluded are drugs that may have shown in vitro activity but currently have no relevant indications listed in this pipeline. This does not apply to phase 1 drugs, whose indications are often unknown. Four drugs are listed as 'possibly' according to these criteria. Data from in vitro studies and mouse models suggest that TP-271 and TP-6076 could potentially meet the criteria for this column. It is suspected that OP0595 will meet the criteria for this column, but is listed as 'possibly' pending identification of the beta-lactam antibiotic with which it will be combined. Similarly, there are currently no publicly available in vitro data for WCK 5222; however, information found in company press releases and trial registrations suggests that this product will meet the criteria for this column. Delafloxacin is also listed as 'possibly.' Although current data show the potential for improved coverage compared with currently available fluoroquinolones in acidic environments, it is not clear how this in vitro benefit will translate into clinical efficacy. This column focuses on only one area of unmet medical need. However, stakeholders often highlight resistant Gram-negative ESKAPE pathogens as an area in which innovation is urgently needed and drug discovery and development are particularly challenging. This column is based on information available in the literature, but we welcome any additional information a company may be able to provide. The column definition was revised in March 2015. In previous versions of this chart, the column included all drugs with Gram-negative activity (including drugs active against *Neisseria gonorrhoeae* or *Haemophilus influenzae*).

4 A 'yes' in this column indicates a drug with the potential to address one of the pathogens identified by the Centers for Disease Control and Prevention as an urgent threat to public health. These include *C. difficile*, carbapenem-resistant Enterobacteriaceae, and drug-resistant *N. gonorrhoeae*. Excluded are drugs that may have shown in vitro activity but currently have no relevant indications listed in this pipeline. This does not apply to phase 1 drugs, where indications are often unknown. Delafloxacin, TP-271, and WCK 5222 are listed as 'possibly' in this column, for the same reasons as explicated in Note 3. Finafloxacin, OP0595, and omadacycline are also listed as 'possibly.' These drugs have in vitro activity against Enterobacteriaceae; however, published studies have not specifically referenced whether these drugs were tested against carbapenem-resistant strains.

5 Based on clinical trials currently registered in clinicaltrials.gov and/or reported qualified infectious disease product (QIDP) designations unless otherwise noted. Bolded text specifies reported QIDP designations. QIDP designations are given by the Food and Drug Administration to antibiotics intended to treat serious or life-threatening infections. QIDPs are eligible to receive benefits under the Generating Antibiotic Incentives Now Act (signed into law as part of the Food and Drug Administration Safety and Innovation Act), including expedited FDA review and extended exclusivity for approved products.

6 Not currently registered on clinicaltrials.gov. Information obtained from the company via a corporate website, news release, and/or direct communication.

7 Avibactam is a new beta-lactamase inhibitor being tested in conjunction with three individual antibiotics. We list two of the combinations here. Another combination, Avycaz, was approved by the FDA in February 2015.

8 Nemonoxacin has been approved for community-acquired bacterial pneumonia in Taiwan, Province of China, and in China.

9 Taksta was granted an orphan drug designation for the indication of prosthetic joint infections.

10 Registered in clinicaltrials.gov but with no current study sites within the United States.

11 In February 2015, FDA approved an otic suspension formulation of finafloxacin to treat acute otitis externa. Because a systemic formulation of finafloxacin has not received approval in the U.S., this drug remains listed in our pipeline.

12 Phase 2 trials for finafloxacin do not currently include any U.S. study sites; however, the company indicated in a December 2012 press release that the trial was based on updated guidance from FDA.

13 Finafloxacin has shown the potential for improved activity under certain conditions, namely acidic environments. Additionally, a company press release noted that phase 2 complicated urinary tract infection study results have shown improved clinical outcomes in patients treated with finafloxacin compared to patients treated with the current standard of care.

14 The phase 2 clinical trial for MRX-I has no specific U.S. study sites listed, but the FDA is listed as the Health Authority for this study.

15 This drug has received QIDP designation, but the specific indication this designation applies to is unknown.

16 This is considered a novel drug class. A novel drug class is defined as a core chemical structure (scaffold) that has not previously been used systemically as an antibacterial in humans.

17 This is considered a novel target. A target is defined as novel if the drug acts on a bacterial structure that has not previously been targeted by a systemic antibacterial in humans.

18 Vaborbactam is a cyclic boronate β-lactamase inhibitor and is combined with a previously approved carbapenem. β-lactamase inhibitors have been paired with β-lactams in the past, but this β-lactamase inhibitor has a novel chemical structure.

19 SPR741 is an antibiotic potentiator that makes the outer membrane of Gram-negative bacteria more permeable, increasing the entry and, therefore, the efficacy of small molecule antibiotics. The antibiotic that SPR741 will be paired with has not yet been announced.

Sources

i Citeline, "Pharmaprojects" (2012), http://www.citeline.com/products/pharmaprojects.

ii U.S. National Institutes of Health, "Search for Studies," http://www.clinicaltrials.gov.

iii Helen W. Boucher et al., "10 x '20 Progress—Development of New Drugs Active Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America," *Clinical Infectious Diseases*56, no. 12 (2013): 1685–94, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3707426.

iv Michael J. Pucci and Karen Bush, "Investigational Antimicrobial Agents of 2013," *Clinical Microbiology Reviews* 26 (2013): 792–821, http://cmr.asm.org/content/26/4/792.

v Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Sept. 16, 2013), http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf.

For further information, please visit:

pewtrusts.org/antibiotic-pipeline

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