Antibiotics Currently in Clinical Development

As of September 2015, an estimated 39 new antibiotics[1] with the potential to treat serious bacterial infections are in clinical development for the U.S. market and two have been approved within the last year. The success rate for clinical drug development is low; at best, only 1 in 5 candidates 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	Development phase[2]	Company	Drug class	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Ceftolozane+Tazobactam (Zerbaxa)	Approved Dec. 19, 2014	Cubist Pharmaceuticals, Inc. (wholly owned subsidiary of Merck & Co.)	Novel cephalosporin+beta-lactamase inhibitor	Yes	No	*Approved for:* **complicated urinary tract infections, complicated intra-abdominal infections,** acute pyelonephritis (kidney infection); *other potential indications:* **hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia**
Ceftazidime+Avibactam (Avycaz)	Approved Feb. 25, 2015[13]	Allergan plc (formerly Actavis)/AstraZeneca plc	Cephalosporin + novel beta-lactamase inhibitor	Yes	Yes	*Approved for:* **complicated urinary tract infections, complicated intra-abdominal infections,** acute pyelonephritis (kidney infection); *other potential indications:* **hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia,** bacteremia
WCK 4873	Phase 1	Wockhardt Ltd.		No	No	Bacterial infections[17]
MGB-BP-3	Phase 1[10]	MGB Biopharma Ltd.		No	Yes	*C. difficile* infections
OP0595 (RG6080)	Phase 1[10]	Meiji Seika Pharma Co., Ltd./Fedora Pharmaceuticals, Inc. (Roche licensee)	Beta-lactamase inhibitor	Possibly	Possibly	Bacterial infections
Aztreonam+Avibactam[7] (ATM-AVI)	Phase 1[10]	AstraZeneca/Allergan (formerly Actavis)	Monobactam + novel beta-lactamase inhibitor	Yes	Yes	Bacterial infections
BAL30072	Phase 1	Basilea Pharmaceutica Ltd.	Monosulfactam	Yes	Yes	Multidrug-resistant Gram-negative bacterial infections[6]
CRS3123	Phase 1	Crestone, Inc.	Methionyl-tRNA synthetase (MetRS) inhibitor	No	Yes	*C. difficile* infections

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LCB01-0371	Phase 1[10]	LegoChem Biosciences, Inc.	Oxazolidinone	No	No	Bacterial infections
TD-1607	Phase 1	Theravance Biopharma, Inc.	Glycopeptide-cephalosporin heterodimer	No	No	**Acute bacterial skin and skin structure infections,[6] hospital-acquired pneumonia/ ventilator-associated pneumonia,[6] bacteremia[6]**
WCK 2349	Phase 1	Wockhardt Ltd.	Fluoroquinolone (WCK 771 pro-drug)	No	No	Bacterial infections[17]
WCK 771	Phase 1	Wockhardt Ltd.	Fluoroquinolone	No	No	Bacterial infections[17]
MRX-I	Phase 2[16]	MicuRx Pharmaceuticals, Inc.	Oxazolidinone	No	No	Acute bacterial skin and skin structure infections
Debio 1450	Phase 2	Debiopharm Group	FabI inhibitor (Debio 1452 pro-drug)	No	No	**Acute bacterial skin and skin structure infections (staphylococci-specific)**
ETX0914	Phase 2	Entasis Therapeutics, Inc.	Spiropyrimidinetrione DNA gyrase inhibitor	No	Yes	**Uncomplicated gonorrhea**
S-649266	Phase 2	Shionogi, Inc.	Cephalosporin	Yes	Yes	Complicated urinary tract infections
POL7080	Phase 2[10]	Polyphor Ltd.	Macrocycle (protein epitope mimetic) LptD inhibitor	Yes (*Pseudomonas*)	No	**Ventilator-associated bacterial pneumonia (caused by *Pseudomonas aeruginosa*),** lower respiratory tract infection, bronchiectasis
Debio 1452	Phase 2	Debiopharm Group	FabI inhibitor	No	No	**Acute bacterial skin and skin structure infections (staphylococci-specific)**
Avarofloxacin	Phase 2	Allergan plc (formerly Actavis)	Fluoroquinolone	No	No	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections**
Brilacidin	Phase 2	Cellceutix Corp.	Defensin-mimetic	No	No	**Acute bacterial skin and skin structure infections**
Ceftaroline+Avibactam	Phase 2	AstraZeneca plc/Allergan plc (formerly Actavis)	Cephalosporin + novel beta-lactamase inhibitor	Yes	Yes	Bacterial infections[6]
CG400549	Phase 2	CrystalGenomics, Inc.	FabI inhibitor	No	No	Acute bacterial skin and skin structure infections, osteomyelitis[6]
Finafloxacin[11]	Phase 2[12]	MerLion Pharmaceuticals Pte Ltd.	Fluoroquinolone	Yes[14]	Possibly[15]	**Complicated urinary tract infections, acute pyelonephritis (kidney infection), complicated intra-abdominal infections, acute bacterial skin and skin structure infections**
Gepotidacin (GSK2140944)	Phase 2	GlaxoSmithKline plc	Novel bacterial topoisomerase inhibitor	No	Yes	Respiratory tract infections, acute bacterial skin and skin structure infections, uncomplicated urogenital gonorrhea

Drug name	Development phase[2]	Company	Drug class	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Nemonoxacin[8]	Phase 2	TaiGen Biotechnology Co., Ltd.	Quinolone	No	No	**Community-acquired bacterial pneumonia,** diabetic foot infection, **acute bacterial skin and skin structure infections**
Radezolid	Phase 2	Melinta Therapeutics, Inc.	Oxazolidinone	No	No	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia**
Ramoplanin	Phase 2	Nanotherapeutics, Inc.	Glycolipodepsipeptide	No	Yes	*C. difficile* relapse prevention[6]
Zabofloxacin	Phase 2	Dong Wha Pharmaceutical Co., Ltd	Fluoroquinolone	No	No	Community-acquired bacterial pneumonia
SMT 19969	Phase 2	Summit Therapeutics, Inc.		No	Yes	***C. difficile*-associated diarrhea**
Omadacycline	Phase 3	Paratek Pharmaceuticals, Inc.	Tetracycline	Yes	Possibly[15]	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections, complicated urinary tract infections**
Lefamulin (BC-3781)	Phase 3	Nabriva Therapeutics AG	Pleuromutilin	No	No	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia,** hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia, osteomyelitis,[6] prosthetic joint infections[6]
Imipenem/ cilastatin+relebactam (MK-7655)	Phase 3[16]	Merck & Co., Inc.	Carbapenem + novel beta-lactamase inhibitor	Yes	Yes	**Complicated urinary tract infections,** acute pyelonephritis, **complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia**
Iclaprim	Phase 3[18]	Motif Bio plc	Dihydrofolate reductase (DHFR) inhibitor	No	No	**Acute bacterial skin and skin structure infections; hospital-acquired bacterial pneumonia**
Cadazolid	Phase 3	Actelion Pharmaceuticals Ltd	Quinolonyl-oxazolidinone	No	Yes	***C. difficile*-associated diarrhea**
Taksta (Fusidic acid)[9]	Phase 3	Cempra, Inc.	Fusidane	No	No	Prosthetic joint infections, **acute bacterial skin and skin structure infections**
Carbavance (RPX7009+meropenem)	Phase 3	Rempex Pharmaceuticals, Inc. (wholly owned subsidiary of The Medicines Co.)	Meropenem + novel boronic beta-lactamase inhibitor	Yes	Yes	**Complicated urinary tract infections, complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia, febrile neutropenia,** bacteremia, acute pyelonephritis (some indications specifically target infections caused by carbapenem-resistant Enterobacteriaceae)

Drug name	Development phase[2]	Company	Drug class	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
Delafloxacin	Phase 3	Melinta Therapeutics, Inc.	Fluoroquinolone	Possibly	Possibly	**Acute bacterial skin and skin structure infections,** hospital-acquired bacterial pneumonia,[6] complicated urinary tract infections,[6] complicated intra-abdominal infections[6]
Eravacycline	Phase 3	Tetraphase Pharmaceuticals, Inc.	Tetracycline	Yes	Yes	**Complicated intra-abdominal infections, complicated urinary tract infections,** hospital-acquired bacterial pneumonia[6]
Plazomicin	Phase 3	Achaogen, Inc.	Aminoglycoside	Yes	Yes	**Complicated urinary tract infections, catheter-related bloodstream infections, hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia, complicated intra-abdominal infections,** acute pyelonephritis (kidney infection) (some indications specifically target infections caused by carbapenem-resistant Enterobacteriaceae)
Solithromycin	Phase 3	Cempra, Inc.	Macrolide (fluoroketolide)	No	Yes	**Community-acquired bacterial pneumonia, uncomplicated urogenital gonorrhea,** urethritis[6]
Surotomycin	Phase 3	Cubist Pharmaceuticals, Inc. (wholly owned subsidiary of Merck & Co.)	Lipopeptide	No	Yes	***C. difficile*-associated diarrhea**

For definitions of drug development terms, visit: http://www.pewtrusts.org/en/research-and-analysis/analysis/2014/03/12/from-lab-bench-to-bedside-a-backgrounder-on-drug-development.

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

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.

* Michael Hay et al., "Clinical Development Success Rates for Investigational Drugs," *Nature Biotechnology* 32, no. 1 (2014): 40–51, doi:10.1038/nbt.2786. 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, Sept. 16, 2013, http://www.cdc.gov/drugresistance/threat-report-2013/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, *H. 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 (*Enterobacter* species, *Klebsiella pneumoniae, Acinetobacter baumanii,* or *Pseudomonas aeruginosa*) 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. Two drugs are listed as 'possibly' according to these criteria. It is suspected that OP0595 will meet the criteria for this column, but is listed as 'possibly' pending public release of data and identification of the beta-lactam antibiotic with which it will be combined. 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 and OP0595 are listed as 'possibly' in this column, for the same reasons as explicated in Note 3. Finafloxacin and omadacycline are also listed as 'possibly' (see Note 15).
5. Based on clinical trials currently registered in clinicaltrials.gov and/or reported qualified infectious disease product (QIDP) designations unless otherwise noted. Bolded indications are 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 all three combinations here.
8. Nemonoxacin has been approved for community-acquired bacterial pneumonia in Taiwan; a new drug application was submitted 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 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 news release that the trial was based on updated guidance from FDA.
13. Avycaz was approved based on Phase 2 data.
14. 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 (unpublished) have shown improved clinical outcomes in patients treated with finafloxacin compared to patients treated with the current standard of care.
15. Both finafloxacin and omadacycline have *in-vitro* activity against Enterobacteriacea; however, published studies have not specifically referenced whether these drugs were tested against carbapenem-resistant strains.
16. These drugs have no specific U.S. study sites listed for one or more clinical trials, but the FDA is listed as the Health Authority for these studies.
17. These drugs have received QIDP designations, but the specific indication this designation applies to is unknown.
18. Iclaprim previously failed to gain approval from the FDA. Current sponsor, Motif Bio, received approval for a new clinical development program from the FDA and plans to resume development for this product. However, there was no new Phase 3 trial in clinicaltrials.gov as of September 2015.

Citations

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

ii. BioCentury, "Antibiotics NCE Pipeline," accessed Oct. 28, 2013, http://www.biocentury.com/antibioticsncepipeline.htm.

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

iv. 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 (2013): 1685–94, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3707426.

v. 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.

vi. 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.

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