Antibiotics Currently in Clinical Development

As of September 15, 2014, an estimated 38 new antibiotics[1] with the potential to treat serious bacterial infections are in clinical development for the U.S. market. The success rate for drug development is low; at best, only 1 in 5 candidates that enter human testing will be approved for patients.* This snapshot of the antibiotic pipeline will be updated periodically as products advance or are known to drop out of development. Please contact Rachel Zetts at rzetts@pewtrusts.org or 202-540-6557 with additions or updates.

Drug name	Development phase[2]	Company	Drug class	Cited for potential activity against gram-negative pathogens?[3]	Known QIDP[4] designation?	Potential indication(s)?[5]
Tedizolid	Approved (for acute bacterial skin and skin structure infections), June 20, 2014	Cubist Pharmaceuticals	Oxazolidinone		Yes	**Acute bacterial skin and skin structure infections, hospital-acquired bacterial pneumonia/ventilator-acquired bacterial pneumonia**
Dalbavancin	Approved, May 23, 2014	Durata Therapeutics	Lipoglycopeptide		Yes	**Acute bacterial skin and skin structure infections**
Oritavancin	Approved, August 6, 2014	The Medicines Company	Glycopeptide		Yes	**Acute bacterial skin and skin structure infections**
Ceftolozane+tazobactam[8]	New Drug Application (NDA) submitted (for complicated urinary tract infection and complicated intra-abdominal infection indications)	Cubist Pharmaceuticals	Novel cephalosporin+beta-lactamase inhibitor	Yes	Yes	**Complicated urinary tract infections, complicated intra-abdominal infections,** acute pyelonephritis (kidney infection), **hospital-acquired bacterial pneumonia/ ventilator-associated pneumonia**
Debio 1450	Phase 1	Debiopharm Group	FabI inhibitor (Debio 1452 pro-drug)		Yes	**Acute bacterial skin and skin structure infections**
AZD0914	Phase 1	AstraZeneca	DNA gyrase inhibitor	Yes	Yes	**Uncomplicated gonorrhea**
Aztreonam+avibactam[7] (ATM-AVI)	Phase 1	AstraZeneca/Forest Laboratories	Monobactam+novel beta-lactamase inhibitor	Yes		Bacterial infections
BAL30072	Phase 1	Basilea Pharmaceutica	Monosulfactam	Yes		Multidrug-resistant Gram-negative bacterial infections[6]
CRS3123	Phase 1	Crestone	Methionyl-tRNA synthetase (MetRS) inhibitor			*Clostridium difficile* infection

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EDP-788	Phase 1	Enanta Pharmaceuticals	Bicyclolide			Bacterial infections
LCB01-0371	Phase 1[11]	LegoChem Biosciences (South Korea)	Oxazolidinone			Bacterial infections
MRX-I	Phase 1	MicuRx Pharmaceuticals	Oxazolidinone			Bacterial infections including community-acquired MRSA and vancomycin-resistant enterococci infections[6]
TD-1607	Phase 1	Theravance Biopharma	Glycopeptide-cephalosporin heterodimer			Serious Gram-positive bacterial infections (acute bacterial skin and skin structure infections, hospital-acquired pneumonia/ventilator-associated pneumonia, bacteremia)[6]
WCK 2349	Phase 1	Wockhardt	Fluoroquinolone (WCK 771 pro-drug)		Yes	Bacterial infections
WCK 771	Phase 1	Wockhardt	Fluoroquinolone		Yes	Bacterial infections
POL7080	Phase 2	Polyphor (Roche licensee)	Macrolide (protein epitope mimetic) LptD inhibitor	Yes (*Pseudomonas*)		Ventilator-associated bacterial pneumonia, lower respiratory tract infection, bronchiectasis
Debio 1452	Phase 2	Debiopharm Group	FabI inhibitor		Yes	**Acute bacterial skin and skin structure infections**
Avarofloxacin	Phase 2	Furiex Pharmaceuticals (acquired by Forest Laboratories)	Fluoroquinolone	Yes	Yes	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections**
Brilacidin	Phase 2	Cellceutix	Defensin-mimetic			Acute bacterial skin and skin structure infections
Ceftaroline+avibactam[8]	Phase 2	AstraZeneca/Forest Laboratories	Cephalosporin+novel beta-lactamase inhibitor	Yes		Complicated urinary tract infections
CG-400549	Phase 2	CrystalGenomics	FabI inhibitor			Acute bacterial skin and skin structure infections, osteomyelitis[6]
Finafloxacin	Phase 2	MerLion Pharmaceuticals	Fluoroquinolone	Yes	Yes	**Complicated urinary tract infections, acute pyelonephritis (kidney infection), acute intra-abdominal infections, acute bacterial skin and skin structure infections**
GSK2140944	Phase 2	GlaxoSmithKline	Type 2 topoisomerase inhibitor			Respiratory tract infections, acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia
Lefamulin (BC-3781)	Phase 2	Nabriva Therapeutics	Pleuromutilin			Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia[6]

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Relebactam (MK-7655)+(imipenem/cilastatin)[8]	Phase 2	Merck	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**
Nemonoxacin[9]	Phase 2	TaiGen Biotechnology	Quinolone	Yes	Yes	**Community-acquired bacterial pneumonia,** diabetic foot infection, **acute bacterial skin and skin structure infections**
Omadacycline	Phase 2	Paratek Pharmaceuticals	Tetracycline	Yes	Yes	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections, complicated urinary tract infections**
Radezolid	Phase 2	Melinta Therapeutics	Oxazolidinone	Yes	Yes	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia**
Ramoplanin	Phase 2	Nanotherapeutics	Lipoglycopeptide			*C. difficile*-associated diarrhea,[6] *C. difficile* relapse prevention[6]
TAKSTA (fusidic acid)[10]	Phase 2	Cempra Pharmaceuticals	Fusidane			Prosthetic joint infections
TD-1792	Phase 2	Theravance	Glycopeptide-cephalosporin heterodimer			Acute bacterial skin and skin structure infections, other serious infections caused by Gram-positive bacteria including hospital-acquired pneumonia/ventilator-associated pneumonia and bacteremia[6]
Zabofloxacin	Phase 2	Dong Wha Pharmaceutical	Fluoroquinolone			Community-acquired bacterial pneumonia
SMT 19969	Phase 2	Summit			Yes	***C. difficile*-associated diarrhea**
Cadazolid	Phase 3	Actelion Pharmaceuticals	Quinolonyl-oxazolidinone		Yes	***C. difficile*-associated diarrhea**
Carbavance	Phase 3	Rempex Pharmaceuticals (wholly owned subsidiary of The Medicines Company)	Carbapenem (biapenem)+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)
Ceftazidime+avibactam (CAZ-AVI)[8]	Phase 3	AstraZeneca/Forest Laboratories	Cephalosporin+novel beta-lactamase inhibitor	Yes	Yes	**Complicated urinary tract infections, complicated intra-abdominal infections,** acute pyelonephritis (kidney infection), **hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia**

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Delafloxacin	Phase 3	Melinta Therapeutics	Fluoroquinolone	Yes	Yes	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia, uncomplicated gonorrhea,** hospital-acquired bacterial pneumonia,[6] complicated urinary tract infections,[6] complicated intra-abdominal infections[6]
Eravacycline[8]	Phase 3	Tetraphase Pharmaceuticals	Tetracycline	Yes	Yes	**Complicated intra-abdominal infections, complicated urinary tract infections,** hospital-acquired bacterial pneumonia[6]
Plazomicin[8]	Phase 3	Achaogen	Aminoglycoside	Yes		Bloodstream infections and nosocomial pneumonia caused by carbapenem-resistant Enterobacteriaceae
Solithromycin	Phase 3	Cempra Pharmaceuticals	Macrolide (ketolide)	Yes	Yes	**Community-acquired bacterial pneumonia, uncomplicated urogenital gonorrhea**
Surotomycin	Phase 3	Cubist Pharmaceuticals	Lipopeptide		Yes	***C. difficile*-associated diarrhea**

Note: The following drugs have been removed from the pipeline:

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 R&D 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. This drug will be included in future updates if development resumes.

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

Notes

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). We excluded biological products, vaccines, and locally acting drugs such as topical, ophthalmic, and inhaled products. Also excluded were drugs used to treat mycobacterial infections such as tuberculosis and *Mycobacterium avium* complex, *H. Pylori*, and biothreat pathogens. 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. 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. Based on information provided on the company website or press releases or based on inclusion in citations iv or v below. "Yes" in this category means that the antibiotic has potential activity against at least one Gram-negative organism. Examples include: the pathogen that causes gonorrhea, *Neisseria gonorrhoeae*, which the CDC classified as an urgent public health threat; Gram-negative bacilli such as members of the Enterobacteriaceae family such as *Klebsiella pneumoniae* and *Escherichia coli*; Acinetobacter species and Pseudomonas species; and so-called fastidious Gram-negative bacteria that commonly cause community-acquired respiratory infections.
4. Certain antibiotics intended to treat serious or life-threatening infections can be designated by the Food and Drug Administration as qualified infectious disease products, or QIDPs. 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.
5. Based on clinical trials currently registered in clinicaltrials.gov and/or reported QIDP designations unless otherwise noted. Bolded indications are reported QIDP designations.

6. Not currently registered in clinicaltrials.gov. Information obtained from the company via a corporate website, press 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. Identified as antibiotics in advanced development (phase 2 or 3) with the potential to treat infections caused by Gram-negative bacilli (Enterobacteriaceae, *Pseudomonas,* Acinetobacter) resistant to currently available treatments. According to the Infectious Diseases Society of America, multidrug-resistant strains of these organisms represent today's most pressing medical threat.
9. Approved for community-acquired bacterial pneumonia in Taiwan, marketing application submitted in China.
10. TAKSTA was granted an orphan drug designation for the indication of prosthetic joint infections.
11. Registered in clinicaltrials.gov, but with no current study sites within the United States.

Citations

i. Citeline, "Pharmaprojects," Pipeline (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 Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America," *Clinical Infectious Disease* 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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