Antibiotics Currently in Clinical Development

As of December 2014, an estimated 37 new antibiotics[1] that have 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 (Sivextro)	Approved June 20, 2014	Cubist Pharmaceuticals	Oxazolidinone		Yes	***Approved for:*** **acute bacterial skin and skin structure infections; *other potential indications:* hospital-acquired bacterial pneumonia/ventilator-acquired bacterial pneumonia**
Dalbavancin (Dalvance)	Approved May 23, 2014	Actavis (formerly Durata Therapeutics)	Lipoglycopeptide		Yes	***Approved for:*** **acute bacterial skin and skin structure infections; *other potential indications:*** community-acquired bacterial pneumonia
Oritavancin (Orbactiv)	Approved Aug. 6, 2014	The Medicines Company	Glycopeptide		Yes	***Approved for:*** **acute bacterial skin and skin structure infections caused by Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA)**
Ceftolozane+Tazobactam (Zerbaxa)	Approved Dec. 19, 2014	Cubist Pharmaceuticals	Novel cephalosporin+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 pneumonia**
Ceftazidime+Avibactam (CAZ-AVI)	New Drug Application (NDA) submitted (for complicated urinary tract infections and complicated intra-abdominal infections)	AstraZeneca/Actavis (formerly 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**
OP0595 (RG 6080)	Phase 1[10]	Meiji Seika Pharma Co. Ltd./Fedora Pharmaceuticals Inc. (Roche licensee)[12]	Beta-lactamase inhibitor	Yes		Bacterial infections

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Debio 1450	Phase 1	Debiopharm Group	FabI inhibitor (Debio 1452 pro-drug)		Yes	**Acute bacterial skin and skin structure infections (staphylococcal-specific)**
Aztreonam+Avibactam[7] (ATM-AVI)	Phase 1[10]	AstraZeneca/Actavis (formerly 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
LCB01-0371	Phase 1[10]	LegoChem Biosciences (South Korea)	Oxazolidanone			Bacterial infections
MRX-I	Phase 1	MicuRx Pharmaceuticals	Oxazolidinone			Acute bacterial skin and skin structure infections
TD-1607	Phase 1	Theravance Biopharma	Glycopeptide-cephalosporin heterodimer		Yes	**Acute bacterial skin and skin structure infections,[6] hospital-acquired pneumonia/ ventilator-associated pneumonia,[6] bacteremia[6]**
WCK 2349	Phase 1	Wockhardt	Fluoroquinolone (WCK 771 pro-drug)		Yes	Bacterial infections
WCK 771	Phase 1	Wockhardt	Fluoroquinolone		Yes	Bacterial infections
AZD0914	Phase 2	AstraZeneca	DNA gyrase inhibitor	Yes	Yes	**Uncomplicated gonorrhea**
S-649266	Phase 2	Shionogi	Cephalosporin	Yes		Complicated urinary tract infections
POL7080 (RG 7929)	Phase 2[10]	Polyphor (Roche licensee)	Macrocycle (protein epitope mimetic) LptD inhibitor	Yes (*Pseudomonas*)	Yes	**Ventilator-associated bacterial pneumonia (caused by *Pseudomonas aeruginosa*),** lower respiratory tract infection, bronchiectasis
Debio 1452	Phase 2	Debiopharm Group	FabI inhibitor		Yes	**Acute bacterial skin and skin structure infections (staphylococcal-specific)**
Avarofloxacin	Phase 2	Actavis (formerly Furiex Pharmaceuticals)	Fluoroquinolone	Yes	Yes	**Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections**
Brilacidin	Phase 2	Cellceutix	Defensin-mimetic		Yes	**Acute bacterial skin and skin structure infections**
Ceftaroline+Avibactam	Phase 2	AstraZeneca/Actavis (formerly Forest Laboratories)	Cephalosporin + novel beta-lactamase inhibitor	Yes		Bacterial infections[6]

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CG-400549	Phase 2	CrystalGenomics	FabI inhibitor			Acute bacterial skin and skin structure infections, osteomyelitis[6]
Finafloxacin	Phase 2[13]	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	Yes		Respiratory tract infections, acute bacterial skin and skin structure infections, uncomplicated urogenital gonorrhea
Lefamulin (BC-3781)	Phase 2	Nabriva Therapeutics	Pleuromutilin	Yes	Yes	**Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia,** hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia[6]
Imipenem/ cilastatin+relebactam (MK-7655)	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[8]	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]
Zabofloxacin	Phase 2	Dong Wha Pharmaceutical	Fluoroquinolone	Yes		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**
Taksta (Fusidic acid)[9]	Phase 3	Cempra Inc.	Fusidane			Prosthetic joint infections, acute bacterial skin and skin structure infections[6]

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Carbavance (RPX709+meropenem)	Phase 3	Rempex Pharmaceuticals (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)
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	Phase 3	Tetraphase Pharmaceuticals	Tetracycline	Yes	Yes	**Complicated intra-abdominal infections, complicated urinary tract infections,** hospital-acquired bacterial pneumonia[6]
Plazomicin	Phase 3	Achaogen	Aminoglycoside	Yes	Yes[11]	**Catheter-related bloodstream infections, hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia, complicated intra-abdominal infections, complicated urinary tract infections** (some indications specifically target infections caused by carbapenem-resistant Enterobacteriaceae)
Solithromycin	Phase 3	Cempra Inc.	Macrolide (fluroketolide)	Yes	Yes	**Community-acquired bacterial pneumonia, uncomplicated urogenital gonorrhea,** urethritis[6]
Surotomycin	Phase 3	Cubist Pharmaceuticals	Lipopeptide		Yes	***C. difficile*-associated diarrhea**

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

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 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—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. See more at http://www.pewtrusts.org/en/multimedia/data-visualizations/2014/antibiotics-currently-in-clinical-development#sthash.XLzMLQta.dpuf.

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 also limited this pipeline 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, we excluded biological products, vaccines, and locally acting drugs such as topical, ophthalmic, and inhaled products. 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 Centers for Disease Control and Prevention classified as an urgent public health threat; Gram-negative bacilli such as members of the Enterobacteriaceae family, including *Klebsiella pneumonia* and *Escherichia coli; Acinetobacter* species and *Pseudomonas* species; and so-called fastidious Gram-negative bacteria that commonly cause community-acquired respiratory infections. In the next update of this pipeline, this column will be split into two in order to specifically highlight those drugs that meet an unmet medical need—specifically those that target Gram-negative bacilli resistant to currently available antibiotics.
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 (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 on 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. Approved for community-acquired bacterial pneumonia in Taiwan; new drug application 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. Plazomicin received the QIDP designations after the December review, but before this update was published.
12. This licensing deal was announced after the December review, but before this update was published.
13. Phase 2 trials 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 the U.S. Food and Drug Administration.

Citations

i. Citeline, 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 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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