Entasis Therapeutics Inc

Small/medium-sized enterprise
Stock exchange: NASDAQ • Ticker: ETTX • HQ: Massachusetts, USA • Employees: 33

PERFORMANCE

Entasis performs well in Research & Development when compared to other small and medium-sized enterprises in scope.

R&D: Entasis has four antibacterial projects for priority pathogens in its pipeline, including one late-stage candidate that is considered novel: zoliflodacin, for uncomplicated *N. gonorrhoeae*. Reports access and stewardship plans for all of its late-stage projects.

SALES AND OPERATIONS

Therapeutic areas: Drug-resistant Gram-negative bacteria
Products on the market: None
R&D grants received since 2016: At least USD 4.5 million, awarded by one funder for two projects (CARB-X). These awards were granted in March and October 2017 to support the development of ETX0282 and the company’s non-beta-lactam PBP (NBP) inhibitor programme, both targeting Gram-negative infections.

Financing and Investment Structure: Entasis is a publicly listed company. It completed its IPO in September 2018, raising USD 75 million, following three funding series, raising USD 105.4 million. Its lead investor was Clarus Ventures.

M&A since 2018: None in the antibacterial and/or antifungal sectors

PIPELINE for diseases in scope

Pipeline size: 4 projects for priority pathogens* (4 antibacterial medicines)
Development stages: 3 clinical projects, including sulbactam/durlobactam, a Phase III fixed-dose combination of a beta-lactamase inhibitor (durlobactam) with the PBP inhibitor sulbactam to treat multidrug-resistant *A. baumannii* infections, and 1 pre-clinical project
Novelty: 1 novel project, zoliflodacin, a Phase II clinical candidate for the treatment of uncomplicated gonorrhoea that belongs to a new chemical class of antibacterials and has a new mode of action and no known cross-resistance to other antibacterial classes
Regulatory approvals: 0 approvals for priority pathogens
Access plans: 2 of 2 late-stage R&D projects with project-specific access plans, including equitable pricing strategies through access-oriented licensing agreements and a partnership with GARDP
Stewardship plans: 2 of 2 late-stage R&D projects with a project-specific stewardship plan in place to continue ongoing surveillance studies for zoliflodacin in partnership with GARDP

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.
OPPORTUNITIES FOR ENTASIS

Expand access and stewardship plans for sulbactam/durlobactam. Entasis’ access and stewardship plans for one of its late-stage candidates, zoliflodacin, represent a good practice. For sulbac- tam/durlobactam, Entasis has already committed to addressing affordability through an equitable pricing strategy and signed an agreement with Zai Lab in China to ensure access to countries in scope in Asia and is actively seeking more partners to license in other regions of the world. In this commitment to find new partners, Entasis has the opportunity to license to other regions of the world. Also in this commitment to find new partners, there is additional opportunity to expand stewardship provisions beyond surveillance.

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT Evaluated: medicine & vaccine pipelines for priority* bacteria & fungi

A.1 R&D investments
Entasis invested USD 58.7 million in the development of antibacterial medicines in 2017 and 2018. As with all other small and medium-sized enterprises (SMEs) evaluated, Entasis was not scored in this indicator.

A.2.1 Pipeline size of four projects
Entasis reports four projects targeting priority pathogens in its pipeline. The company focuses on antibacterial medicine development, and has three projects in clinical development, and one in pre-clinical development.

A.2.2 One clinical-stage novel project
Entasis’ clinical-stage medicine pipeline for priority pathogens consists of both new and adapted R&D projects. Entasis has one clinical-stage antibacterial medicine project that is considered novel: zoliflodacin, for uncomplicated N. gonorrhoeae, which belongs to a new chemical class and has a new mode of action and no cross-resistance to existing classes of antibacterials.

A.2.3 Vaccines in the pipeline
Entasis is not eligible for this indicator as it is not active in vaccine development.

A.2.4 Four candidates targeting critical and/or urgent priorities
Entasis’ clinical pipeline includes a combination medicine candidate in Phase III (sulbactam/dur- lobactam) that targets Carbapenem-resistant A. baumannii (CRAB); a compound in Phase I (ETX0282/cefpodoxime) that targets CRE; and zoliflodacin** in Phase II, being developed with GARDP and that targets N. gonorrhoeae. The company’s pre-clinical pipeline includes one further candidate that targets Gram-negative pathogens considered critical and/or urgent R&D priorities for limiting AMR, as identified by WHO and/or the US Centers for Disease Control and Prevention (CDC).

A.3 Intellectual capital sharing
Entasis reports six intellectual capital sharing initiatives. It engages with different universities and research centres to share molecules and drug analogues in order to identify research lead candidates. In addition, it reports that its agreement with Zai Lab and GARDP includes different examples of intellectual property sharing in terms of manufacturing and commercialisation. As an SME, Entasis was not scored for this indicator, in line with the external stakeholder consensus defined by the Foundation.

A.4 Access and/or stewardship plans for two projects
Entasis has two late-stage R&D projects targeting priority pathogens. For zoliflodacin, Entasis has entered a contract with GARDP (a not-for-profit R&D organisation), enabling GARDP to provide access to and promote the responsible use of zoliflodacin in 168 countries. For sulbac- tam/durlobactam, Entasis is partnering with Zai Lab to conduct clinical trials and obtain regulatory approval in China and other countries belonging to the Association of Southeast Asian Nations (ASEAN), in parallel to the US and Europe. For sulbactam/durlobactam, Entasis is seeking commercial partners to ensure access in low- and middle-income countries. For both projects, Entasis commits to addressing affordability through equitable pricing strategies. Further, Entasis is one of the three SMEs evaluated in the Benchmark that is active in antimicrobial surveillance.

Pipeline targeting priority pathogens: 4 As at 16 October 2019

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
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<tbody>
<tr>
<td>Non-beta-lactam PBP (NBP) inhibitor programme - GNB (including P. aeruginosa)</td>
<td>ETX0282/cefpodoxime - Multidrug-resistant GNB (including CRE) - cUTI</td>
<td>Zoliflodacin** (ETX0914) - N. gonorrhoeae - Uncomplicated gonorrhoea - Novel</td>
<td>Sulbactam/durlobactam - Multidrug-resistant A. baumannii infections</td>
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CRE = Carbapenem-resistant Enterobacteriaceae
GNB = Gram-negative bacteria
PBP = Penicillin-binding protein
cUTI = Complicated urinary tract infection
CRAB = Carbapenem-resistant A. baumannii
CREA = Carbapenem-resistant Pseudomonas aeruginosa

** After the period of analysis, the project has moved to Phase II.

CHANGES SINCE 2018

- Increased its investment in antibacterial development from USD 10-20 million in 2016 to USD 58.7 million in 2017-2018.
- Completed Phase I trial in June 2019 for its oral beta-lactamase inhibitor ETX0282 in combination with cefpodoxime.
- Initiated Phase III trial in April 2019 for its antibacterial sulbactam/durlobactam (ETX251,451L), targeting carbapenem-resistant A. baumannii infections.
- Initiated Phase III clinical trials for zoliflodacin with GARDP in September 2019 to treat drug-resistant gonorrhoea, including access and stewardship plans.

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.
B RESPONSIBLE MANUFACTURING

As an SME, Entasis is not evaluated in this Research Area. It has no antibacterial products on the market.

C APPROPRIATE ACCESS & STEWARDSHIP

As an SME, Entasis is not evaluated in this Research Area. It has no antibacterial and/or antifungal products on the market.