**Nabriva Therapeutics plc**

**Small/medium-sized enterprise**  
Stock exchange: NASDAQ • Ticker: NBRV • HQ: Dublin, Ireland • Employees: 110

**PERFORMANCE**

Nabriva performs on average in Research & Development when compared to other small and medium-sized enterprises in scope.  
**R&D:** Nabriva has seven antibacterial projects for priority pathogens in its pipeline, including one late-stage candidate that is considered novel: lefamulin (Xenleta™), for community-acquired bacterial pneumonia. Granted approval in 2019 for one antibacterial medicine. Reports no project-specific plans for access or stewardship.

**SALES AND OPERATIONS**

**Therapeutic areas:** Anti-infectives  
**Products on the market:** Lefamulin (Xenleta™) received FDA approval in August 2019, after the period of analysis, to treat community-acquired bacterial pneumonia.  
**R&D grants received since 2016:** None  
**Financing and investment structure:** Nabriva is a publicly listed company. It completed its IPO in September 2015, following one funding series and four venture rounds. Its lead investors were Orbimed, Phase 4 Ventures and Vivo Capital. From its inception in 2006 through August 2019, Nabriva has raised USD 537 million, of which USD 54 million was from non-dilutive sources (grants, business development).  
**M&A since 2018:** In July 2018, Nabriva acquired Zavante Therapeutics, including its lead antibacterial drug candidate, an intravenous injectable form of fosfomycin (Contepo™) for the treatment of complicated urinary tract infections, including acute pyelonephritis.

**PIPELINE for diseases in scope**

**Pipeline size:** 7 projects for priority pathogens* (7 antibacterial medicines)  
**Development stages:** 5 clinical projects, including BC-7013, a Phase I clinical candidate that is a semi-synthetic pleuromutilin derivative for the topical treatment of uncomplicated skin and skin structure infections, and 2 discovery/pre-clinical projects  
**Novelty:** 1 novel project, lefamulin (Xenleta™), which was approved for the treatment of community-acquired bacterial pneumonia after the period of analysis and belongs to a new chemical class of antibacterials and has a new mode of action  
**Regulatory approvals:** 1, for lefamulin (Xenleta™) for the treatment of community-acquired bacterial pneumonia in 2019  
**Access plans:** None of its 3 late-stage R&D projects have project-specific access plans.  
**Stewardship plans:** None of its 3 late-stage R&D medicine projects have project-specific stewardship plans.

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* 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 NABRIVA

Develop and implement access and stewardship plans for lefamulin (Xenleta™). Nabriva received FDA approval for lefamulin in August 2019. Nabriva can work with partners to ensure that this product is widely available and affordable in access countries, while appropriately used globally. Stewardship is particularly important because lefamulin is the first of a new class of antibacterials. As examples of access plans, the company can commit to an equitable pricing strategy and/or look for out-licensing opportunities with multiple manufacturers in low- and middle-income countries. As examples of stewardship plans, the company can commit to decouple sales incentives from sales volumes.

Develop access and stewardship plans for IV fosfomycin for injection (Contepo™). Nabriva has already submitted IV fosfomycin for injection for market approval in Europe and plan to re-submit its NDA to the US FDA in the last quarter of 2019. Nabriva can work with partners to develop plans to ensure that IV fosfomycin will be available, affordable and appropriately used after FDA approval. As examples of access plans, the company can commit to an equitable pricing strategy and/or look for out-licensing opportunities with multiple manufacturers in low- and middle-income countries. As examples of stewardship plans, the company can commit to decouple sales incentives from sales volumes and/or become involved in antibacterial surveillance activities.

## PERFORMANCE BY RESEARCH AREA

### A. RESEARCH & DEVELOPMENT

**Evaluate:** medicine & vaccine pipelines for priority* bacteria & fungi

#### A.1 R&D investments

Nabriva invested USD 131.9 million in the development of antibacterial medicines in 2017 and 2018. As with all other small and medium-sized enterprises (SMEs) evaluated, Nabriva was not scored in this indicator.

#### A.2.1 Pipeline size of seven projects

Nabriva reports seven projects targeting priority pathogens in its pipeline. The company focuses on antibacterial medicine development, with one project in discovery stage, another project in pre-clinical development and five projects in clinical development, including one, fosfomycin (Contepo™), currently unavailable in the US, and which has been submitted for FDA market approval. Another project, lefamulin (Xenleta™), was approved after the close of the Benchmark’s period of analysis.

#### A.2.2 One clinical-stage novel project

Nabriva’s clinical-stage medicine pipeline for priority pathogens consists of both new and adapted R&D projects. Nabriva has one late-stage antibacterial medicine project that is considered novel: lefamulin (Xenleta™), for community-acquired bacterial pneumonia, which belongs to a new chemical class and has a new mode of action. Nabriva received an approval for lefamulin for this indication after the close of the Benchmark’s period of analysis.

#### A.2.3 Vaccines in the pipeline

Nabriva is not eligible for this indicator as it is not active in vaccine development.

#### A.2.4 One candidate targeting critical and/or urgent priorities

Nabriva has filed for first marketing authorisation for its adaptation of fosfomycin (Contepo™) in October 2018. This product targets Enterobacteriaceae, which has been identified as a critical priority for limiting AMR by WHO and as an urgent priority by the US Centers for Disease Control and Prevention (CDC).

### Pipeline targeting priority pathogens: 7

**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>
</tr>
</thead>
<tbody>
<tr>
<td>Pleuromutilin molecule platform – GNB and GPB</td>
<td>Lefamulin (Xenleta™) - Multidrug-resistant GNB (including H. influenzae) and GPB (including MRSA) and atypical bacteria - Adaptation (additional indications) - STIs (e.g. N. gonorrhoeae, M. genitalium), HABP/VABP, osteomyelitis and prosthetic joint infections</td>
<td>BC-7013 - GPB (including MRSA and group A and group B Streptococcus spp.) - uSSSI</td>
<td>Lefamulin (Xenleta™) - Multidrug-resistant GNB (including H. influenzae) and GPB (including MRSA) and atypical bacteria - Adaptation (additional target population: pediatric patients)</td>
<td>IV fosfomycin (Contepo™)** - GNB (including ESBL-producing Enterobacteriaceae) and GPB - Adaptation (new dosing approach) - CUTI</td>
<td>Lefamulin (Xenleta™)** - Multidrug-resistant GNB (including H. influenzae) and GPB (including MRSA) and atypical bacteria - CABP - Novel</td>
</tr>
</tbody>
</table>

* 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.

### CHANGES SINCE 2018

- Received FDA approval in August 2019 for lefamulin (Xenleta™) for the treatment of community-acquired bacterial pneumonia.
- Resubmitted NDA for IV fosfomycin (Contepo™) to the FDA in December 2019.
- Acquired Zavante Therapeutics in July 2019, including its lead antibacterial drug candidate, an intravenous injectable form of fosfomycin for the treatment of complicated urinary tract infections, including acute pyelonephritis.

**IV fosfomycin (Contepo™)** was first submitted to the FDA for approval in January 2019. Nabriva anticipates resubmitting to the FDA early in the fourth quarter of 2019.

**Lefamulin (Xenleta™)** was approved after the period of analysis in August 2019 by the FDA.

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* Abbreviations: **ABSSSI** = Acute bacterial skin and skin-structure infection **CABP** = Community-acquired bacterial pneumonia **CUTI** = Complicated urinary tract infection **ESBL** = Extended-spectrum beta-lactamase **GNB** = Gram-negative bacteria **GPB** = Gram-positive bacteria **HABP** = Hospital-acquired bacterial pneumonia **MRSA** = Methicillin-resistant *Staphylococcus aureus* **STIs** = Sexually transmitted infections **uSSSI** = Uncomplicated skin and skin-structure infection **VABP** = Ventilator-associated bacterial pneumonia
B RESPONSIBLE MANUFACTURING

As an SME, Nabriva is not evaluated in this Research Area. After the period of analysis, Nabriva gained marketing approval for one antibacterial product, lefamulin (Xenleta™). The Benchmark notes that Nabriva has published, in its annual report, the identities of all the suppliers it contracts for the manufacture of both the API and the drug product forms of lefamulin. Nabriva was not scored on these activities.

C APPROPRIATE ACCESS & STEWARDSHIP

As an SME, Nabriva is not evaluated in this Research Area. It has one antibacterial and/or antifungal product on the market: the antibacterial lefamulin (Xenleta™).

A.3 Intellectual capital sharing

As an SME, Nabriva was not scored for this indicator, in line with the external stakeholder consensus defined by the Foundation.

A.4 No access or stewardship plans for late-stage R&D projects targeting priority pathogens

Nabriva has three such R&D projects. It currently reports no plans that address either the stewardship of or appropriate access to the products, upon reaching the market.