This overview covers traditional (direct-acting small molecules) and non-traditional antibacterial agents in clinical and preclinical development worldwide. It assesses to what extent the clinical pipeline addresses World Health Organization (WHO) priority pathogens, *Mycobacterium tuberculosis* and *Clostridioides difficile*.

The current clinical antibacterial pipeline contains 43 antibiotics and combinations with a new therapeutic entity and 27 non-traditional antibacterial agents.

### Clinical Antibacterial Pipeline

Overall, the clinical pipeline and recently approved antibiotics are insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance.
2020 Preclinical Antibacterial Pipeline

Currently there are 162 commercial and non-commercial entities progressing 292 diverse antibacterial agents.

### Categorization of preclinical agents

- **Direct-acting small molecules**: 115 (39.4%)
- **Antimicrobial peptides**: 29 (10.2%)
- **Vaccines**: 47 (16.1%)
- **Non-traditional approaches**: 101 (34.6%)

### Mode of action and development stages

<table>
<thead>
<tr>
<th>Mode of action</th>
<th>LO</th>
<th>PCC</th>
<th>CTA/IND</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell membrane</td>
<td>17</td>
<td>40</td>
<td>5</td>
<td>62</td>
</tr>
<tr>
<td>Immunomodulation</td>
<td>18</td>
<td>34</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>Cell wall synthesis</td>
<td>9</td>
<td>22</td>
<td>9</td>
<td>40</td>
</tr>
<tr>
<td>Protein synthesis</td>
<td>14</td>
<td>9</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>26</td>
</tr>
<tr>
<td>Anti-virulence</td>
<td>13</td>
<td>5</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>DNA replication</td>
<td>10</td>
<td>6</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Cell metabolism</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>RNA synthesis</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>31</td>
<td>18</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

LO=lead optimization; PCC=preclinical candidate; CTA/IND=CTA/IND-enabling studies

### Pathogens targeted by a single pathogen target product

Of the 292 antibacterial agents, 152 (52%) target a single pathogen, of which 60 target the WHO critical priority pathogens:

- *Acinetobacter baumannii* (12)
- *Pseudomonas aeruginosa* (25)
- *Escherichia coli* (12)
- *Klebsiella pneumoniae* (9)
- *Enterobacter spp.* (2)
- *Enterococcus faecium* (1)
- *Helicobacter pylori* (2)
- *Salmonella spp.* (1)
- *Staphylococcus aureus* (18)
- *Campylobacter jejuni* (1)
- *Neisseria gonorrhoeae* (4)
- *Streptococcus pneumoniae* (10)
- *Haemophilus influenzae* (3)
- *Shigella* (3)
- *Mycobacterium tuberculosis* (41)
- *Clostridioides difficile* (8)

### Developers’ type and size

- **Academic**: 11
- **Commercial**: 11
- **Foundation**: 2

The preclinical pipeline is dynamic and innovative, including a wide range of drug development projects that are using different approaches to target the WHO bacterial priority pathogens list.