NovaBiotics
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NovaBiotics®
TAKING NATURE'S LEAD IN ANTIMICROBIALS

Novel approaches to treating medically unmet bacterial and fungal infections and tackling antimicrobial resistance

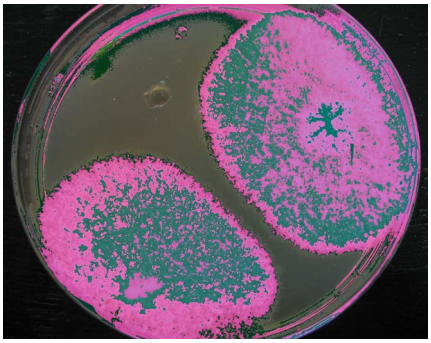
NovaBiotics' platform technologies leverage defense strategies of the innate immune system and provide first-in-class antibacterial and antifungal therapies with potent activity against drug-resistant infections.

Antimicrobial resistance (AMR) is a well-established challenge that has a potentially catastrophic impact both in terms of human health and global economic performance. NovaBiotics, a UK-based biotech with an equal focus on antibacterials and antifungals, is taking a unique approach to addressing AMR in many ways.

NovaBiotics has developed a novel approach to the challenge of infection and AMR by addressing the problem from the host's perspective and harnessing 'AMR status-agnostic' components of the innate immune system that normally deal with infection. In nature, antimicrobial peptides (AMPs) and aminothiols form the cornerstone of the body's first line of defense against the spectrum of potentially harmful microbes with which people come into contact daily. NovaBiotics has developed platforms that can harness the beneficial properties of these natural, infection-fighting agents, which have already yielded novel classes of compounds that target a range of fungal, bacterial and polymicrobial infections. This 'smart immunology' approach has already been useful in other therapeutic conditions, most notably oncology and inflammation. Indeed, eight of the top fifteen best-selling drugs are immune-derived biologics.

Delivering first-in-class drug candidates

NovaBiotics' AMP platform is generating novel, synthetic antibacterial and antifungal peptide drug candidates with membrane-targeted, rapidly microbicidal modes of action. These compounds are derived, but wholly distinct from endogenous AMPs. They share common, highly desirable properties with their endogenous AMP predecessors, including a rapid kill time and activity against a broad range of fungal, bacterial and polymicrobial infections, including multidrug-resistant pathogens, but are synthetic, therapeutically viable, novel peptide structures. While the use of such compounds as potential antimicrobials has been debated and anticipated for some time, the potential of AMP has not yet been fully realized. NovaBiotics has been able been able to re-engineer undruggable host defense peptide structures to create viable antimicrobial candidates that have demonstrated potent activity against so-called ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*



and *Enterobacter* spp.) and other key bacterial pathogens, as well as a range of fungal pathogens including drug-resistant *Candida* spp., *Aspergillus* spp. and other yeasts and moulds.

Preclinical-stage candidates derived from the AMP platform include Novarifyn (NP432), a potent bactericidal peptide that outperforms traditional therapy classes in terms of kill time; Novamycin (NP339), an antifungal peptide with placebo-like safety unheard of in antifungals active against *Aspergillus*, *Cryptococcus* and *Candida* spp., as well as emerging fungal pathogens (anticipated to enter clinical development in 2019); and Luminaderm (NP108), which has demonstrated efficacy in the nasal decolonization of *Staphylococcus* spp. and outperforms the current 'gold-standard' decolonization agent, mupirocin, in its bactericidal activity against methicillin-resistant *S. aureus*.

The company's second platform is underpinned by cysteamine, an endogenous aminothiol produced in mammalian cells as a result of coenzyme A metabolism through the activity of the vanin family of pantetheinase ectoenzymes. Cysteamine has antibiotic, antibiofilm and antivirulence properties, as well as being a potent, broad-spectrum chemopotentiator that improves the performance of other existing antibiotic classes.

The leading drug candidate in NovaBiotics' pipeline to emerge from the cysteamine platform is Lynovex (NM001), which provides a completely novel approach for treating the symptoms of cystic fibrosis (CF)-associated respiratory infections in all CF patients, regardless of *CFTR* genotype and/or mutation status. Lynovex, which is also potently mucolytic and therefore represents a breakthrough in CF treatment, has orphan drug designation in both the US and Europe and fast-track designation in the US. The company is developing two formulations of the molecule: Lynovex Oral, which is currently in phase 2 trials as a treatment for CF exacerbations, and Lynovex Inhaled, a chronic CF therapy that is set to enter clinical development in 2019.

Also derived from the same aminothiol platform as Lynovex, NovaBiotics is developing Nylexa (NM002), an antibiotic potentiator and resistance-breaking agent with utility and scope against drug-resistant (even multidrug-resistant and extensively drug-resistant) bacterial infections that boosts and reinvigorates the effectiveness of poorly perfoming or 'defunct' (because of resistance) antibiotics (as well as being an antibiotic in its own right).

Pipeline and platform potential

"Drug candidates from both platforms have mechanisms of action that are agnostic to the antimicrobial resistance status of target pathogens and minimize, if not negate, the development of future acquired resistance," said Deborah O'Neil, CEO of NovaBiotics.

NovaBiotics has a track record in establishing successful commercial partnerships (its topical peptide antifungal for fungal nail infection, Novexatin, was outlicensed to Taro Pharmaceuticals in 2013, and an oral form of cysteamine for cystic fibrosis exacerbations was outlicensed to an undisclosed partner in 2016). "The deals we have done to date are focused on two very specific products from each of our platforms in niche indications and we are now shifting the emphasis towards the fact that we have developed more 'mainstream' antimicrobials from the two platforms. These are very commercially attractive products for use against Gram-negative and positive ESKAPE bacterial pathogens (peptides and cysteamine) and moulds and yeasts (peptides). The value of the platforms is worth more than the sum of their individual 'parts'. Both sets of technology are highly complementary, but are wholly independent platforms," O'Neil added.

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