amplyx

APX001 FACT SHEET

Overview

Fungi are adaptable microorganisms present in the environment and are part of the normal flora of humans and animals. They can cause diseases in humans that range from mild superficial infections of the skin and mucous membranes to severe, invasive and life-threatening infections. Patients with compromised immune systems from an underlying disease (e.g. leukemia, HIV) or treatment (immunosuppressive agents post solid organ transplant, anti-inflammatory drugs) are susceptible to infections which quickly become life threatening if they are not treated promptly with effective treatments. Over 600,000 cases of invasive fungal infections occur annually, caused primarily by *Candida* and *Aspergillus* fungi.

There are four classes of antifungal drugs: polyenes, fluorinated pyrimidines, azoles and echinocandins; none of which have the optimal antifungal drug charcteristics to successfully treat serious invasive fungal infections. The reasons for treatment failure include poor safety profile, drug-drug interactions, fungi resistance, variable pharmacokinetics or lack of a suitable formulation. Invasive infections due to *Aspergillus, Fusarium, Scedosporium* and fungi from the Mucorales order (e.g. *Mucor* spp. and *Rhizopus* spp.) are especially problematic to treat. Consequently, invasive fungal infections are associated with high mortality rates (50-80%), even when patients receive treatment. Most concerning, as with multidrug-resistant bacteria, the frequency of fungi resistant to both the azole and candin class are increasingly being recognized. Thus, there remains a significant unmet medical need for a new broad spectrum antifungal to treat serious, invasive fungal infection and reduce the existing high morbidity and mortality.

APX001 has a unique mechanism of action and exhibits broad spectrum activity against pathogenic molds including Mucorales, Aspergillus (including non-fumigatus species), Scedosporium and Fusarium, which are often resistant to the currently available antifungal agents.

APX001 Product Highlights

Amplyx Pharmaceuticals is developing APX001, a novel, broad-spectrum antifungal agent for the treatment of life-threatening invasive fungal infections, including rare, difficult-to-treat molds. APX001 is available in both an IV and oral formulation which enable rapid IV treatment within the hospital setting with continued oral treatment after discharge. Both formulations have been well tolerated, with a favorable safety profile in Phase 1 studies and a low propensity for clinically important drug-drug interactions.

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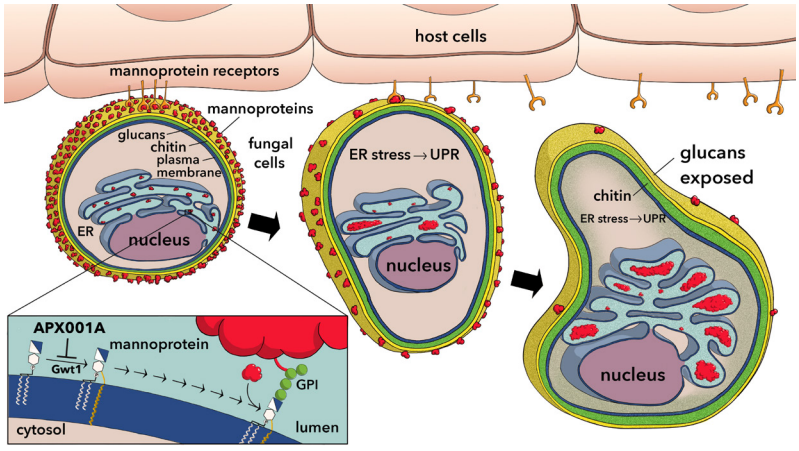
APX001A Inhibits the Fungal Gwt1 Protein

- Gwt1 is essential for trafficking and anchoring mannoprotein to the outer cell wall
- Mannoproteins are required for cell wall integrity, adhesion, pathogenicity, and evading the host immune system
- APX001A has many physiological effects including deficiency in hyphal formation, malformation of cell size and shape, adhesion, reduction in cell wall-linked mannoproteins, biofilm formation, exposure of the glucan layer and ER stress



APX001 Data Highlights

APX001 is the prodrug of APX001A, which is a first-in-class small molecule with a unique mechanism of action that inhibits the fungal enzyme Gwt1 that is part of glycosylphosphatidylinositol (GPI) biosynthesis. The GPI pathway is responsible for post-translational modification and cell surface localization of proteins that anchor the fungal cell wall and provide cell wall integrity. Since the GPI pathway is present in all fungi inhibition of GPI biosynthesis presents an attractive target for the development of a broad-spectrum antifungal drug to treat the major fungal pathogens, including *Candida* and *Aspergillus.*

APX001A has been evaluated extensively in preclinical studies, and it exhibits broad spectrum activity against pathogenic yeasts (e.g. *Candida* spp.) and molds (e.g. *Aspergillus* spp.) including multi drug resistant strains and the rare, hard-to-treat molds (e.g. *Fusarium, Scedosporium* and fungi from the Mucorales order). APX001 has demonstrated good activity in animal models of invasive candidiasis, invasive aspergillosis and invasive rare mold infections (scedosporiosis, fusariosis and mucormycosis). A comprehensive nonclinical safety program has been conducted to support the safety of APX001 in early clinical development. The results of these studies are consistent with an appropriate therapeutic window.

Data Highlights

- **No significant safety signals in adverse events (AEs), laboratory safety tests, physical exams or ECG**
- **Safe and well tolerated in Phase I studies in doses up to 1000 mg (IV) and 1000 mg (oral)**
- **Pharmacokinetic (PK) parameters of IV and oral formulations are linear and dose proportional**
- **Oral bioavailability of ~90%**
- **Animal model efficacy target $AUC_{0\text{-}24}$ exceeded safely**

Development Status

Phase 1 clinical trials of APX001 are completed. These studies were designed to determine the safety, tolerability and pharmacokinetics of the IV and oral formulations in healthy volunteers. Currently, a Phase 2 study is being conducted in patients with with candidemia, as well as an additional Phase 1b study in patients who are neutropenic (e.g. acute leukemia patients receiving chemotherapy) and at risk of fungal infections. Additional Phase 1 studies are examining drug-drug interaction and drug distribution and elimination (mass balance) in healthy volunteers. In addition, Amplyx aims to conduct a clinical PK study in subjects who have renal or hepatic insufficiency.

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