Tarsus Pharmaceuticals, Inc.
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Tarsus takes on *Demodex* blepharitis with TP-03: a first-in-class, anti-parasitic, investigational therapy

Tarsus is developing its lead candidate TP-03, potentially the first FDA-approved therapy for *Demodex* blepharitis, and a pipeline of investigational therapies targeting eye care, dermatology, and infectious disease prevention, including Lyme disease and malaria.

Recent research indicates that more than half of the 45 million patients who visit eye care clinics in the US each year may have *Demodex* blepharitis; inflammation of the eyelid caused by the most common human ectoparasite, the *Demodex* mite. The recent Atlas study showed that *Demodex* blepharitis can have a clinical, functional and psychosocial impact on patients, with 80% saying it negatively impacted their daily life. However, there is no treatment currently approved by the US Food and Drug Administration (FDA). Tarsus is conducting pivotal trials of TP-03, an eye drop formulation of lotilaner, an antiparasitic that targets the *Demodex* mite, to potentially address this need.

In addition to *Demodex* blepharitis, Tarsus has a pipeline of investigational therapies targeting indications in eye care, dermatology and infectious disease prevention, including Lyme disease and community prevention of malaria. According to Tarsus' President and CEO Bobak Azamian, "Our mission is to focus on unmet needs and apply proven science and new technology to revolutionize treatment for patients, starting with eye care." The company is continuing to advance these programs following a recent IPO that raised gross proceeds of over $100 million.

Mechanism of disease and prevalence

The mite infestation that causes *Demodex* blepharitis is highly prevalent yet often overlooked and misdiagnosed. While the symptoms—red, irritated, itchy eyes—overlap with those of other conditions, *Demodex* blepharitis can be readily distinguished based on the presence of collarettes, or cylindrical dandruff, a pathognomonic sign of the disease, by viewing the base of the upper lid under a slit lamp while the patient looks downward. Collarettes are accumulations of waste from *Demodex* infestation of eyelash follicles (Fig. 1). Blepharitis can also lead to missing or misdirected eyelashes, blurred vision, and inflammation of the cornea.

Despite the lack of FDA-approved treatments, approximately 2.1 million cases of blepharitis are reported annually by ICD-10 code in the United States. Interestingly, ICD code diagnosis of another common ophthalmic condition, dry eye, increased 12-fold with FDA approval of the first drug specific for that condition, reaching more than 6 million diagnoses per year in the US. Similarly, rapid growth in diagnosis of *Demodex* blepharitis may occur should an effective treatment reach the market.

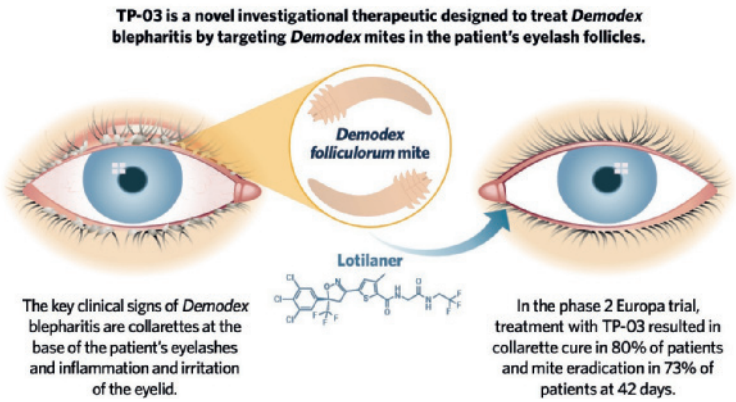

Fig. 1 | Clinical signs of *Demodex* blepharitis and results of treatment with TP-03.

TP-03 clinical program advancing to phase 3

Tarsus' TP-03 investigational therapy specifically targets *Demodex* mites and has been well tolerated and efficacious in four phase 2 clinical trials. Lotilaner, the active ingredient in TP-03, inhibits insect and arachnid GABA-chloride channels, causing parasite paralysis and death. Lotilaner is widely used in veterinary medicine in different formulations and is highly lipophilic, which may allow it to diffuse into lipid-rich glands where *Demodex* thrives. In clinical trials, TP-03 eyedrops taken twice daily met all efficacy endpoints and had no serious adverse events. For example, Europa, a phase 2b randomized controlled trial of TP-03 to treat *Demodex* blepharitis, achieved the trial's primary endpoint of collarette cure (0 to 2 collarettes) in 80% of patients taking TP-03 and the secondary endpoint of mite eradication in 73% by day 42, both a statistically significant difference from patients taking vehicle. Two pivotal trials (Saturn-1 and Saturn-2) will assess these same endpoints in approximately 800 patients. Saturn-1 began enrolling in September 2020 with results expected in July; Saturn-2 just began in May 2021.

Robust pipeline, global reach

Tarsus is planning to initiate a phase 2 proof-of-concept clinical trial with TP-03 for another ophthalmic indication associated with *Demodex*, Meibomian Gland Disease (MGD). In MGD, the meibomian glands lining the edge of the eyelid can be infested with *Demodex* mites. MGD may alter the tear film and is one of the leading causes of dry eye disease. Beyond the eye, Tarsus is developing additional lotilaner formulations to treat or prevent other diseases linked to ectoparasites. These include development of TP-04 (lotilaner topical formulation) for rosacea, where evidence suggests *Demodex* could be a major contributing factor. An investigational new drug (IND) application for an oral tablet formulation, TP-05, was recently accepted by the FDA, clearing the way for Tarsus to begin phase 1 clinical trials for Lyme disease prevention by potentially killing the ticks that carry the *Borrelia* bacteria before they can transmit disease to humans. TP-05 is also being explored for community prevention of malaria.

The company recently entered into an out-licensing agreement with LianBio Ophthalmology Limited (LianBio) to develop and commercialize TP-03 in the People's Republic of China, Hong Kong, Macau, and Taiwan (Greater China). The agreement may provide patients with access to TP-03 in Greater China, where there are as many as 40 million blepharitis and 70 million MGD patients in need. Tarsus may receive up to $200 million in upfront and milestone payments from LianBio, in addition to royalties and a minority equity stake in LianBio upon achievement of certain milestones. Tarsus will continue to drive the development of its pipeline to help meet the worldwide need for effective and safe therapies, harnessing boundless therapeutic ingenuity for patients.

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