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Disclaimer: This press release is a translation of Hengrui Pharma's original release dated March 21, 2023. [8]

**MARKETING AUTHORIZATION APPLICATION FOR DRY EYE DISEASE DRUG SHR8028
(CYCLOSPORINE OPHTHALMIC SOLUTION) DEVELOPED BY JIANGSU HENGRUI
PHARMACEUTICAL HAS BEEN ACCEPTED IN THE PEOPLE'S REPUBLIC OF CHINA**

March 27, 2023. Chengdu Shengdi Pharmaceutical Co., Ltd., a subsidiary of Jiangsu Hengrui Pharmaceuticals Co., Ltd. ("Hengrui Pharma"), recently received the "Notice of Acceptance" from the Chinese National Medical Products Administration (NMPA). The marketing authorization application for SHR8028 (cyclosporine ophthalmic solution) eye drops for the treatment of the signs and symptoms of dry eye disease was accepted by NMPA.

The marketing authorization application is based on a multi-center, randomized, vehicle-controlled, double-blind, phase 3 clinical study (study number SHR8028-301). The results showed that SHR8028 eye drops, compared to its vehicle, significantly improved the signs and symptoms of dry eye disease. At the same time, SHR8028 eye drops were safe, reliable, and well tolerated. The incidence of adverse events and local instillation site reactions after taking the drops were comparable between SHR8028 and the vehicle.

About the SHR8028-301 Study

The SHR8028-301 study is a multi-center, randomized, vehicle-controlled, double-blind, phase 3 clinical study evaluating the efficacy and safety of SHR8028 eye drops for the treatment of dry eye disease. A total of 206 subjects with moderate to severe dry eye disease were randomized 1:1 to receive either SHR8028 eye drops or the vehicle respectively.

The results of the study showed that compared to vehicle, SHR8028 eye drops can significantly improve the signs and symptoms of patients with moderate to severe dry eye disease. This effect was maintained during the viewing period.

About Dry Eye Disease

The International Tear Film & Ocular Surface Society Dry Eye Working Group (TFOS DEWS) defines dry eye disease as a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.[1]

Due to the different definition standards of dry eye disease, the estimated global prevalence of dry eye disease varies greatly between 5.5% to 33.7%.[2] Epidemiological survey data from 2010 showed that the prevalence of dry eye disease in Chinese people aged 5-89 years based on signs and symptoms was 13.6% and based on symptoms only 31.4%. [3] With the acceleration of China's population aging process, changes in people's living environment, lifestyle, and work intensity, as well as the popularization of electronic equipment, it is expected that dry eye disease will occur more frequently. [4]

In the current treatment of dry eye disease, tear replacement with ocular lubricants ("artificial tears") is traditionally considered a mainstay of treatment in China. However, these products often only relieve dry eye symptoms but do not target the underlying pathophysiology of dry eye disease which may lead to symptoms to recur. The 2017 consensus of dry eye experts from the International Tear Film and Ocular Surface Association pointed out that key etiologies of tear film instability, hyperosmolarity, and ocular surface inflammation and damage were determined to be important for inclusion in the definition, thus, has become an important link in the comprehensive management of dry eye. [5]

The Expert Consensus on Dry Eye in China (2020) clearly stated that cyclosporine and other immunosuppressants can be used for moderate to severe dry eye with ocular inflammation, especially for immune-related dry eye.[6]

About SHR8028 eye drops

SHR8028 eye drops (0.1% cyclosporine ophthalmic solution), a topical anti-inflammatory and immunomodulating drug, was introduced by Hengrui Pharma from Novaliq GmbH, Germany. Cyclosporine is a highly potent and selective immunosuppressant used in the treatment of T-cell-mediated ocular surface diseases, such as dry eye. There have been advances in research related to immunomodulatory drugs with anti-inflammatory properties and the ability to reduce inflammatory markers and decrease elevated tear film osmolarity, with promising clinical effects. [5]

SHR8028 eye drops use EyeSol®, a new water-free drug delivery platform based on semifluorinated alkanes (SFAs). The use of the semifluorinated alkane perfluorobutylpentane (F4H5) as a solvent increases the dissolution of cyclosporine in SHR8028 eye drops, and its physical properties make it an optimal solvent for topical ophthalmic formulations. SHR8028 eye drops are free of oils, surfactants, and preservatives with potential benefits including high topical bioavailability, rapid onset of action, good topical tolerance and reduction of visual impairment related to oil-based eye drops, emulsions, or ointments.[7]

SHR8028 has completed several clinical trials and Novaliq, a partner of Hengrui, submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in August 2022 and is currently under review for the proposed indication for the treatment of the signs and symptoms of dry eye disease.

Note:

The text above is a translation into English of the original press release by Hengrui Pharma from March 21, 2023. See [8] for the original version.

About Novaliq

Novaliq is a biopharmaceutical company focusing on the development and commercialization of first- and best-in-class ocular therapeutics based on EyeSol®, the worldwide first water-free technology. Novaliq offers an industry-leading portfolio addressing today's unmet medical needs of millions of patients with eye diseases. In 2019, Hengrui Pharma and Novaliq announced a strategic collaboration under which Hengrui Pharma secured exclusive rights to develop, manufacture, and commercialize NOV03 (local drug name SHR8058 eye drops) and CyclASol® (local drug name SHR8028 Eye Drops) in China. Novaliq GmbH is headquartered in Heidelberg, Germany and Novaliq Inc. has an office in

Cambridge, MA, USA. The long-term shareholder is dievini Hopp BioTech holding GmbH & Co. KG, an active investor in Life and Health Sciences companies. More on www.novaliq.com.

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