Donidalorsen

An **Investigational** RNA-targeted Medicine

Disease Background

Hereditary angioedema (HAE) is a rare and potentially life-threatening genetic condition that involves recurrent attacks of severe swelling (angioedema) in various parts of the body, including the hands, feet, genitals, stomach, face and/or throat. Despite currently available treatment options, **attacks remain unpredictable** for people living with HAE and **can be life-threatening.**[1-6]

Overview

Discovered and developed by Ionis, **donidalorsen is an investigational RNA-targeted LIgand-Conjugated Antisense (LICA) medicine designed to designed to target prekallikrein (PKK),** which plays an important role in activating inflammatory mediators associated with acute attacks of hereditary angioedema (HAE). By reducing the production of PKK, donidalorsen could be an effective prophylactic approach to preventing HAE attacks.[7-10]

In the U.S., doctors frequently use prophylactic treatment approaches to prevent and reduce the severity of HAE attacks. Donidalorsen is being investigated as a potential prophylactic treatment for patients living with HAE.

*Donidalorsen is an **investigational medicine** for which the safety and efficacy have not been evaluated by any regulatory body.*

Phase 3 Clinical Development Program

The Phase 3 clinical development program for donidalorsen is made up of two studies – the pivotal OASIS-HAE study and OASISplus, which includes both a Phase 3 open-label extension (OLE) cohort and switch cohort.

Phase 3 Clinical Development Program *(cont.)*

OASIS-HAE

The global, multicenter, randomized, double-blind, placebo-controlled **Phase 3 OASIS-HAE study** met its primary endpoint, significantly reducing the average monthly HAE attack rate in patients treated with donidalorsen every 4 weeks ($p<0.001$) or 8 weeks ($p=0.004$), compared to placebo.

- The study enrolled 91 participants aged 12 and older with HAE-1 or HAE-2.
- Participants were randomized in a 2:1 ratio to receive donidalorsen 80 mg or placebo via subcutaneous injection once every four weeks for 24 weeks or donidalorsen 80 mg or placebo via subcutaneous injection once every eight weeks for 24 weeks.

Following completion of the placebo-controlled treatment period in OASIS-HAE, 94% of patients entered the OASISplus OLE study.

OASISplus

The **Phase 3 OASISplus study** included **OLE** and **switch** cohorts, designed to help researchers learn if the investigational medicine is safe and effective for people with HAE when given over a long-term period.

- The study enrolled a total of 83 participants aged 12 and older with Type 1 or Type 2 HAE.
- The 53-week global, multicenter trial is evaluating 80 mg subcutaneous injections of donidalorsen administered every four or every eight weeks in patients either:
    - Continuing on from the OASIS-HAE trial, OR
    - Switching over from a different prophylactic therapy
- The OASISplus switch cohort is evaluating the safety and efficacy of long-term dosing of donidalorsen every four weeks in patients who were previously treated with another HAE medication.

Donidalorsen was well-tolerated across both studies. There were no serious treatment emergent adverse events (TEAEs) related to donidalorsen, and most adverse events (AEs) were mild or moderate in severity.

The OASISplus study is ongoing to evaluate donidalorsen as a potential treatment option for people living with HAE.

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