



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

9 January 2020  
EMADOC-628903358-1519

## Public summary of opinion on orphan designation

Combination of two adeno-associated viral vectors of serotype 8 containing the 5'- and the 3'- half coding sequences of human *ABCA4* fused to inteins for the treatment of Stargardt's disease

On 17 October 2019, orphan designation EU/3/19/2208 was granted by the European Commission to Fondazione Telethon, Italy, for combination of two adeno-associated viral vectors of serotype 8 containing the 5'-, the 3'- half coding sequences of human *ABCA4* fused to inteins for the treatment of Stargardt's disease.

### What is Stargardt's disease?

Stargardt's disease is a hereditary disorder of the eye that leads to progressive loss of sight. In most cases Stargardt's disease is caused by abnormalities in a gene called *ABCA4*. The *ABCA4* gene is responsible for the production of a protein called ABCR that regulates the transport of vitamin A byproducts in and out of some cells in the retina (the light-sensitive surface at the back of the eye). In patients with Stargardt's disease, ABCR does not work properly. As a result, deposits known as lipofuscins, made of fats, proteins and harmful vitamin A byproducts, build up inside the retina cells, which become damaged and eventually die.

Stargardt's disease is a long-term debilitating disease, because the patient's sight becomes progressively worse and eventually leads to blindness.

### What is the estimated number of patients affected by the condition?

At the time of designation, Stargardt's disease affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 people\*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).



## What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of Stargardt's disease.

## How is this medicine expected to work?

This medicine is made of two viruses, each containing half of the normal human *ABCA4* gene. When injected into the eye of patients with Stargardt's disease, the viruses will produce the two halves of the protein ABCR which will then re-assemble into normal ABCR protein. This is expected to relieve the symptoms of the disease and prevent loss of sight.

The type of virus used in this medicine ('adeno-associated virus') does not cause disease in humans.

## What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with Stargardt's disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Stargardt's disease or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 12 September 2019, recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

## For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on [EMA website](#).

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;

- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

## Translations of the active ingredient and indication in all official EU languages<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Combination of two adeno-associated viral vectors of serotype 8 containing the 5'- and the 3'- half coding sequences of human <i>ABCA4</i> fused to inteins	Treatment of Stargardt's disease
Bulgarian	Комбинация от два аденоасоциирани вирусни вектора на серотип 8, съдържащи 5' и 3' половината кодиращи последователности на човешки <i>ABCA4</i> , слят с интеини	Лечение на болест на Stargardt
Croatian	Kombinacija dvaju adeno- pridruženih virusnih vektora serotipa 8 koji sadrže 5'- i 3'-polovične kodirajuće sekvence ljudskog <i>ABCA4</i> spojene na intein	Liječenje Stargardtove bolesti
Czech	Kombinace dvou adeno-asociovaných virových vektorů sérotypu 8 obsahujících 5'- a 3'-poloviny kódující sekvence lidského <i>ABCA4</i> fúzované k inteinu	Léčba Stargardtovy choroby
Danish	Kombination af to adenoassocierede virale vektorer af serotype 8 indeholdende 5'- og 3'- halv-kodende sekvenser af humant <i>ABCA4</i> kondenseret til intein	Behandling af Stargardt sygdom
Dutch	Combinatie van twee adeno-geassocieerde virale vectoren van serotype 8 met de 5'- en de 3'-half coderende sequenties van humaan <i>ABCA4</i> gefuseerd met inteïne	Behandeling van de ziekte van Stargardt
Estonian	Kombinatsioon kahest 8. serotüüpi adeno-assotsieerunud viirusvektorist, mis sisaldab inteiniiga fuseeritud inimese <i>ABCA4</i> 3' ja 5' poolseid kodeerivaid järjestusi	Stargardt'tõve ravi
Finnish	Kahden adeno-assosioituneen serotyypin 8 virusvektorin kombinaatio, joka sisältää ihmisen <i>ABCA4</i> :n koodaavat sekvenssit 5'- ja 3' fuusioituna inteiniin	Stargardtin taudin hoito
French	Association de deux vecteurs viraux adéno-associés de sérotype 8 contenant les séquences codantes 5' et 3' de l' <i>ABCA4</i> humain fusionné à l'intine	Traitement de la maladie de Stargardt
German	Kombination von zwei Adeno-assoziierten viralen Vektoren des Serotyps 8, die die 5'- und die 3'-Hälfte codierenden Sequenzen von menschlichem <i>ABCA4</i> enthalten, die an Intein fusioniert sind	Behandlung der Stargardt-Krankheit

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Greek	Συνδυασμός δύο αδeno-συσχετιζόμενων ιικών φορέων οροτύπου 8 που περιέχουν τις αλληλουχίες που κωδικοποιούν το 5'- και το 3'- ήμισυ του ανθρώπινου <i>ABCA4</i> συγχωνευμένο με ιντεΐνες	Θεραπεία της νόσου Stargardt
Hungarian	A humán <i>ABCA4</i> 5'- és 3'-fele kódoló szekvenciáját tartalmazó 8. szerotípusú két adeno-asszociált virális vektor kombinációja inteinnel kondenzáltan	Stargardt-kór kezelése
Italian	Combinazione di due vettori virali adeno-associati di sierotipo 8, contenenti le metà al 5' e 3' del gene <i>ABCA4</i> fuse ad inteina	Trattamento della malattia di Stargardt
Latvian	Divu adeno-saistītu 8. serotipa vīrusu vektoru, kas satur ar inteīniem sapludinātas cilvēka <i>ABCA4</i> 5'- un 3'- pusi kodējošās sekvenses, savienojums	Stargardta slimības ārstēšana
Lithuanian	Dviejų adeno asocijuoto viruso vektorių junginys iš 8 serotipo, turintis 5'- ir 3'- pusę koduojančių žmogaus <i>ABCA4</i> sekų, sulietų su inteinu	Stargardt ligos gydymas
Maltese	Taħlita ta 'żewġ vettori virali assoċjati ma' l-adeno ta 'serotip 8 li fihom is-sekwenzi ta' kodiċi ta '5'- u 3'- nofs ta' l- <i>ABCA4</i> uman imdewba ma 'l-intein	Kura tal-marda ta' Stargardt
Polish	Kombinacja dwóch wektorów wirusowych związanych z adenowirusem serotypu 8 zawierających sekwencje kodujące 5' i 3' ludzkiego genu <i>ABCA4</i> połączone z inteiną	Leczenie choroby Stargardta
Portuguese	Combinação de dois vetores virais adenoassociados do sorotipo 8 contendo as sequências de codificação 5'- e 3'-half do <i>ABCA4</i> humano fundidos a intein	Tratamento da doença de Stargardt
Romanian	Combinăție de doi vectori virali adeno-asociați ai serotipului 8 conținând secvențele de codificare 5'- și 3'-jumătate ale <i>ABCA4</i> umane fuzionate pentru intein	Tratamentul bolii Stargardt
Slovak	Kombinácia dvoch adeno-asociovaných vírusových vektorov sérotypu 8 obsahujúcich 5'- a 3'-polovičnú kódujúcu sekvenciu ľudského <i>ABCA4</i> fúzovaného s inteínom	Liečba Stargardtovej choroby
Slovenian	Kombinacija dveh adeno-povezanih virusnih vektorjev serotipa 8, ki vsebujeta 5'- in 3'-pol kodirne sekvence človeškega <i>ABCA4</i> , pripojene na intein	Zdravljenje Stargardtove bolezni

Language	Active ingredient	Indication
Spanish	Combinacion de dos vectores virales adenoasociados del serotipo 8 que contienen las secuencias codificantes en 5 'y en la mitad 3' de <i>ABCA4</i> humano fusionadas a inteína	Tratamiento de la enfermedad de Stargardt
Swedish	Kombination av två adenoassocierade virala vektorer av serotyp 8 innehållande 5'- och 3'-halva kodande sekvenserna av humant <i>ABCA4</i> kondenserat till intein	Behandling av Stargardts sjukdom
Norwegian	Kombinasjon av to adenoassosierte virusvektorer av serotype 8 som inneholder 5'- og 3'-halvpart av kodende sekvens for humant <i>ABCA4</i> koblet til intein	Behandling av Stargardts sykdom
Icelandic	Blanding av to adeno-assosierte virale vektorer av serotype 8 inneholdende 5'- og 3'-halv-kodende sekvensene av humant <i>ABCA4</i> kondensert til intolerance	Meðferð við Stargardts sjúkdómi