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Public summary of opinion on orphan designation

Antisense oligonucleotide targeting exon 13 in the *USH2A* gene for the treatment of retinitis pigmentosa

On 23 August 2017, orphan designation (EU/3/17/1899) was granted by the European Commission to ProQR Therapeutics IV BV, the Netherlands, for antisense oligonucleotide targeting exon 13 in the *USH2A* gene (also known as QR-421) for the treatment of retinitis pigmentosa.

What is retinitis pigmentosa?

Retinitis pigmentosa is a group of hereditary diseases of the eye that lead to progressive loss of sight. In patients with retinitis pigmentosa, cells in the retina (the light-sensitive surface at the back of the eye) become damaged and eventually die.

Retinitis pigmentosa is a long-term debilitating disease because it causes the patient's sight to get worse, eventually leading to blindness.

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

At the time of designation, retinitis pigmentosa affected approximately 3.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 191,000 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).

What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating retinitis pigmentosa. Patients with the condition were given sunglasses to slow down damage to the retina, genetic counselling (discussion of the risks of passing the condition on to children) and general support.

*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 515,700,000 (Eurostat 2017).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

How is this medicine expected to work?

One form of retinitis pigmentosa is caused by a mutation (change) in the *USH2A* gene responsible for the production of a protein called usherin, which is essential for the normal functioning of retinal cells. This mutation leads to the production of a faulty usherin protein.

This medicine is an 'antisense oligonucleotide', a small strand of synthetic genetic material. It has been designed to attach to the mutated genetic material of retinal cells after injection into the eye, and restore production of a functioning form of usherin. This is expected to result in improvement in the symptoms of the condition.

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, no clinical trials with the medicine in patients with retinitis pigmentosa had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 July 2017 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, on the medicine's rare disease designations page.

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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Antisense oligonucleotide targeting exon 13 in the *USH2A* gene	Treatment of retinitis pigmentosa
Bulgarian	Антисенс олигонуклеотид насочен към екзон 13 на *USH2A* гена	Лечение на пигментен ретинит
Croatian	Protusmjerni oligonukleotid koji cilja egzon 13 u genu *USH2A*	Liječenje retinitisa pigmentoze
Czech	Protisměrný oligonukleotid cílený k exonu 13 *USH2A* genu	Léčba pigmentosní retinitidy
Danish	Antisense oligonucleotid rettet mod exon 13 i *USH2A* genet	Behandling af retinitis pigmentosa
Dutch	Antisense oligonucleotide dat zich richt op exon 13 in het *USH2A* gen	Behandeling van retinitis pigmentosa
Estonian	USH2A geeni 13. eksoni vastu suunatud antisenss oligonukleotiid	Pigmentoosse võrkkestapõletiku ravi
Finnish	Antisense-oligonukleotidi, jonka kohteena on *USH2A*-geenin eksoni 13	Verkkokalvorappeuman hoito
French	Oligonucleotide antisens ciblant l'exon 13 du gène *USH2A*	Traitement de la rétinite pigmentaire
German	Antisense-Oligonukleotid, das auf das Exon 13 des *USH2A* Gens gerichtet ist	Behandlung der Retinopathia Pigmentosa
Greek	Αντιαγγελιαφόρο ολιγονουκλεοτίδιο που στοχεύει το εξώνιο 13 του γονιδίου *USH2A*	Θεραπεία της μελαγχρωστικής αμφιβληστροειδοπάθειας
Hungarian	Az *USH2A* génben levő 13-as exont célzó antiszenz oligonukleotid	Retinitis pigmentosa kezelése
Italian	Oligonucleotide antisenso contro l'esone 13 del gene *USH2A*	Trattamento della retinite pigmentosa
Latvian	Antisensa oligonukleotīds, kas vērsts pret *USH2A* gēna 13. eksonu	*Retinitis pigmentosa* ārstēšana
Lithuanian	Priešprasmis oligonukleotidas nukreiptas į 13-ą *USH2A* geno egzoną	Pigmentinio retinito gydymas
Maltese	Oligonukleotide antisense li timmira exon 13 fil-ġene *USH2A*	Kura tar-retinite pigmentuża
Polish	Antysensowny oligonukleotyd skierowany przeciw eksonowi 13 genu *USH2A*	Leczenie retinopatii barwnikowej
Portuguese	Oligonucleotído anti-senso direcionado para o exão 13 no gene *USH2A*	Tratamento da retinite pigmentosa
Romanian	Oligonucleotidă antisens ţintind exonul 13 al genei *USH2A*	Tratamentul retinitei pigmentare
Slovak	Antisense oligonukleotid zacielený na exón 13 v *USH2A* géne	Liečba retinitis pigmentosa

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Protismerni ologonukleotid za ekson 13 *USH2A* gena	Zdravljenje pigmentozne retinopatije
Spanish	Oligonucleótido antisentido dirigido al exón 13 en el gen *USH2A*	Tratamiento de la retinosis pigmentaria
Swedish	Antisensoligonukleotid mot exon 13 i *USH2A* genen	Behandling av retinitis pigmentosa
Norwegian	Antisense oligonukleotid rettet mot exon 13 i *USH2A* genet	Behandling av retinitis pigmentosa
Icelandic	Antisense ólígónúkleótíð sem beinist gegn exon 13 í *USH2A* geni	Meðferð á retinitis pigmentosa