EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 December 2019
EMADOC-628903358-1299

# Public summary of opinion on orphan designation

## Recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN6* gene for the treatment of neuronal ceroid lipofuscinosis

On 21 August 2019, orphan designation EU/3/19/2197 was granted by the European Commission to Amicus Therapeutics Europe Limited, Ireland, for recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN6* gene (also known as AT-GTX-501) for the treatment of neuronal ceroid lipofuscinosis.

### What is neuronal ceroid lipofuscinosis?

Neuronal ceroid lipofuscinosis is a group of inherited diseases where deposits known as lipofuscins made of fats and proteins build up in the brain and other parts of the body, such as the eye, causing damage. Symptoms of the disease include delayed speech, inability to coordinate muscle movements, fits, loss of vision and mental disability.

Neuronal ceroid lipofuscinosis is a debilitating and life-threatening condition that leads to death by early adulthood.

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

At the time of designation, neuronal ceroid lipofuscinosis affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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, the medicine Brineura was authorised in the EU for the treatment of neuronal ceroid lipofuscinosis type 2. Brineura replaces the TPP1 enzyme (one of several proteins

*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).

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whose absence can lead to lipofuscin build-up) which is missing in this form of the disease. The disease was also managed by treating its symptoms.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with neuronal ceroid lipofuscinosis because laboratory data show that it may allow treatment of patients with neuronal ceroid lipofuscinosis type 6, which involves a different protein, and for whom no treatment exists. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

## How is this medicine expected to work?

This medicine is expected to be used in patients with neuronal ceroid lipofuscinosis type 6. These patients have mutations (changes) in a gene called *CLN6* that is responsible for the production of a protein needed for the function of the endoplasmic reticulum (ER), a structure in the cell involved in various processes including the breakdown of harmful substances. As a result, the ER does not work properly, leading to build-up of lipofuscins.

This medicine is made of a virus that contains normal copies of the *CLN6* gene. When injected into the patient, it is expected that the virus will be carried into the nerve cells enabling them to start producing a working CLN6 protein. This is expected to restore the function of the ER and relieve the symptoms of the disease.

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?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with neuronal ceroid lipofuscinosis were ongoing.

At the time of submission, recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN6* gene was not authorised anywhere in the EU for the treatment of neuronal ceroid lipofuscinosis 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 18 July 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[1], Norwegian and Icelandic

| Language | Active ingredient | Indication |
|---|---|---|
| English | Recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN6* gene | Treatment of neuronal ceroid lipofuscinosis |
| Bulgarian | Рекомбинантен самокомплементарен адено-асоциран вирусен вектор серотип 9, съдържащ човешкия ген *CLN6* | Лечение на невронална цероидна липофусциноза |
| Croatian | Rekombinantni samo-komplementarni adeno povezani virusni vektor serotipa 9 koji sadrži humani gen *CLN6* | Liječenje neuronske ceroidne lipofuscinoze |
| Czech | Rekombinantní samokomplementární adeno-asociovaný virový vektor sérotypu 9 obsahující lidský gen *CLN6* | Léčba neuronální ceroidní lipofuscinózy |
| Danish | Rekombinant selvkomplementær adenoassocieret virusvektor serotype 9, indeholdende det humane *CLN6*-gen | Behandling af neuronal ceroid lipofuscinose |
| Dutch | Recombinante zelf-complementaire adenogeassocieerde virale vector, serotype 9, die het humane gen *CNL6* bevat | Behandeling van neuronaal ceroïd lipofuscinose |
| Estonian | Rekombinantse ja iseendaga komplementaarse adenoassotsieeruva viirusvektori serotüüp 9, mis sisaldab inimese *CLN6* geeni | Neuronaalse tseroidse lipofustsinoosi ravi |
| Finnish | Rekombinantti, itseään kohti takaisin taittuva adenoassosioitu virusvektori, serotyyppiä 9, joka sisältää ihmisen *CLN6*-geenin | Neuronaalisen seroidilipofuskinoosin hoito |
| French | Vecteur viral adéno-associé auto-complémentaire recombinant de serotype 9 contenant le gène humain *CLN6* | Traitement de la céroïde-lipofuscinose neuronale |
| German | Rekombinanter selbstkomplementärer adeno-assoziierter viraler Vektor vom Serotyp 9, der das menschliche Gen *CLN6* enthält | Behandlung der neuronalen Ceroid-Lipofuszinose |
| Greek | Ανασυνδυασμένος αυτοσυμπληρωματικός αδενο-σχετιζόμενος ιϊκός φορέας οροτύπου 9 που περιέχει το ανθρώπινο γονίδιο *CLN6* | Θεραπεία της Νευρωνικής Κηροειδούς Λιποφουσκίνωσης |
| Hungarian | Humán *CLN6* gént tartalmazó 9-es szerotípusú rekombináns önmagával komplementer adenoasszociált vírusvektor | Neuronális ceroid lipofuscinosis kezelése |
| Italian | Vettore virale adeno-associato autocomplementare ricombinante del sierotipo 9 contenente il gene umano *CLN6* | Trattamento della ceroido lipofuscinosi neuronale |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Latvian | Rekombinants pašpapildinošs adenosaistītā vīrusa vektora 9. serotips, kas satur cilvēka *CLN6* gēnu | Neironu ceroīdās lipofuscinozes ārstēšana |
| Lithuanian | Rekombinantinis, pats sau komplimentarus, su adeno virusu susietas 9 serotipo virusinis vektorius, turintis žmogaus *CLN6* geną | Neuronų ceroidinės lipofuscinozės gydymas |
| Maltese | Serotip ta' vetturi vjurali rikombinanti adeno-assoċjati self-komplimentari 9 li fih il-ġene *CLN6* uman | Kura taċ-ċerojdu lipofuxinosi newronali |
| Polish | Rekombinowany samo-komplementarny wektor wirusowy związany z adenowirusami serotypu 9 zawierający ludzki gen *CLN3* | Leczenie ceroidolipofuscynozy neuronalnej |
| Portuguese | Vetor viral adeno-associado de serotipo 9 recombinante e auto-complementar que contém o gene humano *CLN6* | Tratamento da lipofuscinose ceróide neuronal |
| Romanian | Vector viral adeno-asociat recombinant autocomplementar de serotip 9 ce conține gena umană *CLN6* | Tratamentul lipofuscinozei ceroide neuronale |
| Slovak | Rekombinantný samo-komplementárny adeno-asociovaný vírusový vektor sérotypu 9 obsahujúci ľudský gén *CLN6* | Liečba neuronálnej ceroidnej lipofuscinózy |
| Slovenian | Rekombinantni samokomplementarni adenovirusom pridruženi virusni vektor serotipa 9,ki vsebuje človeški gen *CLN3* | Zdravljenje nevronalne ceroidne lipofuscinoze |
| Spanish | Vector viral adenoasociado autocomplementario recombinante del serotipo 9 que contiene el gen humano *CLN6* | Tratamiento de la lipofuscinosis neuronal ceroidea |
| Swedish | Rekombinant självkomplementär adenoassocierad virusvektor, serotyp 9, innehållande den mänskliga *CLN6*-genen | Behandling av neuronal ceroidlipofuscinos |
| Norwegian | Rekombinant selvkomplementær adenoassosiert virusvektor serotype 9 som inneholder det humane *CLN6*-genet | Behandling av nevronal ceroid lipofuscinose |
| Icelandic | Raðbrigða sjálffyllandi eitlatengd veiruferja af sermisgerð 9 sem kóðar fyrir manna *CLN6* geni | Meðferð við taugaceróíð lípófúskinósis |