Prosensa is working towards long-term access to drisapersen

Leiden, August 15 2014

Dear Patient Group Representative,

As previously communicated, Prosensa received guidance from the United States Food and Drug Administration (FDA) on June 2, in which a regulatory pathway for accelerated approval was outlined for drisapersen. Based on this guidance, we communicated that we intend to submit a file to the FDA later this year and will commit to the initiation of two confirmatory post-approval studies, as recommended by the FDA (to be commenced prior to an approval). We also have ongoing interactions with the European Medicines Agency (EMA), and we anticipate filing for a conditional approval in the EU shortly after the submission of a New Drug Application to the FDA. We are encouraged by the flexibility recently shown by both FDA and EMA, regarding products for DMD.

Prosensa is currently focusing on the preparation of the New Drug Application for submission to the FDA later this year. This is always a monumental undertaking, as New Drug Applications are typically made up of about 100,000 pages which display the results of all of the available clinical and pre-clinical trials as well as the analysis and interpretation of this data. Information about the manufacturing and quality control of the drug is also included.

One of the confirmatory post-approval studies will be an open-label study with drisapersen where the results will be compared with a natural history control group. A Prosensa natural history study is already ongoing and fully recruited with 269 participants. The other confirmatory post-approval study for drisapersen will be a placebo-controlled study with one of our other exon-skipping investigational compounds for DMD. For this study Prosensa will choose one product out of its clinical products PRO044, PRO045 and PRO053. Prosensa is working hard to finalize the study design of the confirmatory studies. We anticipate commencing both confirmatory studies in the first half of 2015 and will have more information on the study design and protocols in the coming months.

	Phase I/II clinical trial	**Phase III trial**
PRO044	Completed Extension study on track to start Q4 2014	Placebo-controlled trial Anticipated to start H1 2015 in US, EU and potentially other countries.
PRO045	Dose finding study ongoing; 4 cohorts completed Data expected Q4 2014	Placebo-controlled trial or open-label trial Anticipated to start in 2015 in US, EU and potentially other countries.
PRO053	Dose finding study ongoing; 2 cohorts completed Data expected H1 2015	Placebo-controlled trial or open-label trial Anticipated to start in 2015 in US, EU and potentially other countries.

PRO052 and PRO055 are in advanced preclinical development. PROSPECT is in early pre-clinical development and applies multiple exon skipping focused on the exon 10-30 region.

For the drisapersen re-dosing program, we are on track for re-dosing the first boys prior to the end of September. The re-dosing protocols for this group have been finalized both for North America and

Europe, sent to the relevant health authorities and we have begun the process of submitting to the relevant Institutional Review Boards (IRBs) at the hospitals of the participating sites for local ethics approval. For individual centers the starting date will also be dependent on the time it takes to gain the necessary IRB approval.

As communicated earlier, in North America eligible boys are those who completed DEMAND V (DMD114876), those that are currently in the DMD115501 protocol and US/Canadian boys who participated in the DEMAND IV study (DMD114349). In the first week of August, Prosensa organized an investigator meeting for the participating sites, which aimed to discuss the final protocol and logistics for conducting the study. We anticipate to start entering boys into the re-dosing program early September and to re-dose the boys from the first sites to get IRB approval around mid-September. The burden of participating in the open label re-dosing program is significantly lower for boys and their families compared to the original studies. Subjects will initially be dosed in the clinic for the first 4 weeks, but home dosing is intended, subject to site requirements. Since the primary aim of the re-dosing program is to provide access to drisapersen, no biopsies will be taken under this protocol.

In Europe, eligible boys are those that participated in the long-term CLIN-02 study (DMD114673). Pending final regulatory approvals, re-dosing for this first group is also scheduled to begin before the end of September and will be done under the existing treatment protocol. An amended protocol will be used to reduce the burden for participating boys and their families. As communicated before, re-dosing of boys that participated in drisapersen studies will take a staged approach. Prosensa intends to provide access for all patients that previously participated in the drisapersen studies, provided safety criteria are met. We are looking into the possibilities for re-dosing of the remaining studies on a country by country basis and are currently working on expected timelines for the next group of countries.

A dedicated page at the Prosensa website www.prosensa.eu/patients-and-family/drisapersen-re-dosing enables easier tracking of the latest information regarding the drisapersen re-dosing program that is publicly available. Families and patients that have previously participated in drisapersen clinical trials are encouraged to remain in contact with the investigator at their site, who is their primary point of contact.

With kind regards,

Giles Campion, MD – Chief Medical Officer and SVP Research & Development

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