

## FINAL REPORT - LAY SUMMARY

### A NEW METHOD FOR THE DETERMINATION OF A GM1-GANGLIOSIDOSIS-SPECIFIC BIOMARKER

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Beta-galactosidase, the enzyme which is deficient in GM1-gangliosidosis, is involved in the degradation of several cell constituents, such as GM1-gangliosides, keratan sulfate and oligosaccharides attached to glycoproteins. In the absence of beta-galactosidase, these cell constituents accumulate in cells, organs and body fluids, such as plasma and urine and, ultimately, lead to the somatic features associated with the condition.

A sensitive method was developed by the Greenwood Genetic Center for the determination of an oligosaccharide (*i.e.* a structure made of 5 sugar units) which is elevated only in cells and urine of GM1-gangliosidosis patients. As this component is highly soluble in water, it is readily found in urine of patients, constituting thereby a convenient biomarker.

As this promising GM1-gangliosidosis-specific biomarker is found in cells and in urine of patients, it could be exploited for:

- The unambiguous identification of GM1-gangliosidosis patients and those responding to drug candidates. The test consists in the culture of white cells isolated from a small blood sample in the presence of the drug candidate, followed by the determination of the oligosaccharide in cell lysates. A decrease in the oligosaccharide level indicates that the patient carries beta-galactosidase mutations responding to the drug candidate.
- Monitoring the efficacy of novel therapeutic interventions for GM1-gangliosidosis patients. Determination of the biomarker in urine would allow the clinicians to rapidly adjust the dosage of the drug candidate.
- The further development of the small molecule currently conducted by DORPHAN, and which may provide therapeutic relief for a subset of GM1-gangliosidosis patients.

The characterization of this new GM1-gangliosidosis biomarker therefore constitutes an important element in the preparation of a first in man evaluation of the drug candidate DORPHAN is currently developing.

The financial support of the NTSAD has provided has helped to further our drug candidate as the first therapy for GM1-gangliosidosis.