February 2019

BioMarin Sanfilippo Syndrome Type B (MPS IIIB) Clinical Development Program

We would like to update you regarding our clinical development program in Sanfilippo B. The BioMarin program, which involves multiple centers around the world, consists of three studies and is described below.

The first study is an **observational study** of children with Sanfilippo B, between the ages of 1 and 10 years old and includes testing of cognitive and adaptive function. The observational study lasts for 48-96 weeks. The tests explore how the child thinks and acquires new information as well as how the child deals with daily living. There are also assessments of behavior and quality of life. This study is intended to provide baseline information about how children with Sanfilippo B progress in the absence of treatment. This baseline information may then be compared to disease progression information from BioMarin's treatment study (both for individual children and in aggregate).

The observational study is being conducted at sites in Australia, Colombia, Germany, Spain, Taiwan, Turkey, UK and USA. Enrollment into this study is now complete.

For more details, please visit: https://clinicaltrials.gov/show/NCT02493998

The second study is a **treatment study** in which children with Sanfilippo B receive an investigational enzyme replacement therapy, this used to be called BMN250 but is now known as tralesinidase alfa. The enzyme is administered directly into the brain as an infusion via a surgically implanted device. To enroll in the treatment study, a child must have completed the observational study as outlined above. This study is being conducted at the same sites. Children who have previously received an investigational drug as part of another clinical study, including gene therapy, may not be enrolled in this study.

For more details, please visit: https://clinicaltrials.gov/show/NCT02754076

The third study is a **natural history study** of children with Sanfilippo B up to 18 years old, who do not meet the criteria for participation in the observational study. Children enrolled into this study do not receive the investigational treatment. The objective of this study is to better understand the natural course of Sanfilippo B. This study is actively enrolling new participants and is being conducted in Australia, Brazil, Colombia, Germany, Spain, Taiwan, Turkey and USA.

For more details, please visit: https://clinicaltrials.gov/ct2/show/NCT03227042

Your child's doctor remains the best source of information regarding the care of your child and any questions or concerns should be directed to your child's doctor.

If you represent a patient association, please contact BioMarin Patient Advocacy patientadvocacy@bmrn.com. Alternatively, please email BioMarin Medical Information medinfo@bmrn.com

For more information about active clinical studies, including Sanfilippo SyndromeType B, please visit www.clinicaltrials.gov or https://www.clinicaltrialsregister.eu/.

May 2018

BioMarin Sanfilippo Syndrome Type B (MPS IIIB) Program Update

We would like to update you about the status of our clinical development program in Sanfilippo B. The BioMarin program, which involves multiple centers around the world, consists of three studies, described below.

The first study is an observational study of children with Sanfilippo B and includes testing of cognitive and adaptive function. The observational study lasts for 48 weeks. The tests explore how the child thinks and acquires new information as well as how the child deals with daily living. There are also assessments of behavior and quality of life. This study is intended to provide baseline information about how children with Sanfilippo B progress in the absence of treatment. This baseline information may then be compared to disease progression information from BioMarin's treatment study (both for individual children and in aggregate).

The observational study is being conducted at sites in Australia, Colombia, Germany, Spain, Taiwan, Turkey, UK and USA. Enrollment to this study is now complete.

For more details, please visit: https://clinicaltrials.gov/show/NCT02493998

The second study is a treatment study in which children with Sanfilippo B will receive an investigational enzyme replacement therapy, known as BMN 250. The enzyme is administered directly to the brain as an infusion via a surgically implanted port. To enroll in the treatment study, a child must have completed the observational study as outlined above. This study is being conducted at the same centers. Children who have previously received an investigational drug as part of another clinical study, including gene therapy, may not be enrolled in this study.

For more details, please visit: https://clinicaltrials.gov/show/NCT02754076

The third study is a natural history study of children with Sanfilippo B up to 18 years old, who do not meet the criteria for participation in the observational study. Children enrolled into this study do not receive the investigational treatment. The objective of this study is to better understand the natural course of Sanfilippo B.

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January 2018

BioMarin Sanfilippo Syndrome Type B (MPS IIIB) Program Update

We have received a number of inquiries regarding our clinical development program in Sanfilippo Syndrome Type B (MPS IIIB) and we would like to update you about the status of this program. The BioMarin program which involves multiple centers around the world, is open and is actively enrolling. The program consists of three studies, described below.

The first study is an observational study of children with Sanfilippo B and includes testing of cognitive and adaptive function. The observational study lasts for 48 weeks. These tests explore how the child thinks and acquires new information as well as how the child deals with daily living. There are also assessments of behavior and quality of life. This study is intended to provide baseline information about how children with Sanfilippo B progress in the absence of treatment. This baseline information can then be compared to disease progression information from BioMarin's treatment study (both for individual children and in aggregate). This study is enrolling children 1-10 years old.

The observational study is enrolling at sites in Australia, Colombia, Germany, Spain, Taiwan, Turkey, UK and USA.

For more details please visit: https://clinicaltrials.gov/show/NCT02493998

The second study is a treatment study in which children with Sanfilippo Type B will receive an investigational enzyme replacement therapy, known as BMN 250. The enzyme is administered directly to the brain as an infusion via a surgically implanted port. To enroll in the treatment study, a child must have completed the observational study as outlined above. This study is being conducted at the same centers. At present, children who have previously received an investigational drug as part of another clinical study, including gene therapy, may not be enrolled in this study.

For more details please visit: https://clinicaltrials.gov/show/NCT02754076

The third study is a natural history study of children with Sanfilippo B up to 18 years old, who do not meet the criteria for participation in the observational study. Children enrolled on this study do not receive the investigational treatment. The objective of this study is to better understand the natural course of Sanfilippo B.

For more details please visit: https://clinicaltrials.gov/ct2/show/NCT0322704

MMRC/BMN25/0027

Any questions or concerns you may have should be directed to your child's doctor, who remains the best source of information about the care of your child.

To contact BioMarin please email BioMarin Medical Information medinfo@bmrn.com or BioMarin Patient Advocacy patientadvocacy@bmrn.com

For more information about active clinical studies, including Sanfilippo Type B, please visit www.clinicaltrials.gov or https://www.clinicaltrialsregister.eu/