Vaccine’s to the Rescue!

Hope everyone is having a wonderful summer – especially since most of our OA children *(ages 12 and up)* are finally receiving the COVID-19 vaccine. What a great feeling! Below are a few photos from some of OAA warriors who were one of the first to receive their vaccinations in March/April!

Be sure to read the Research Update on the new treatments for MMA/PA:

Since COVID is behind us – we have **THREE** clinical trials actively recruiting for new treatments for MMA/PA! Information available on ClinicalTrials.gov and an update from these Pharmaceutical companies are located in the “Research Update” of this issue!

OAA is hosting another virtual webinar in August - New therapies for combined D, L-2-hydroxyglutaric acidemia and isovaleric acidemia. Families are eager to hear about upcoming new treatments and appreciate OAA medical advisor, Dr. Jerry Vockley sharing what he and his team have been working on. We appreciate all of our medical advisors and researchers for tirelessly working on new treatments and cures for our children!

Registration required: [https://us02web.zoom.us/webinar/register/WN_BNro3nxvRhy-UEUfh9gpHA](https://us02web.zoom.us/webinar/register/WN_BNro3nxvRhy-UEUfh9gpHA)

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## Medical Advisors

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Olaf Bodamer FACMG</td>
<td>Boston Children’s Hospital 539, 300 Longwood Ave. Boston, MA 02215</td>
</tr>
<tr>
<td>Mark Korson, MD VMP Genetics, LLC Director of Physician Support Director of Education 5579 Chamblee Dunwoody Road Suite 110 Atlanta, GA 30338</td>
<td></td>
</tr>
<tr>
<td>Stephen Cederbaum, MD</td>
<td>Mental Retardation Research Ctr/NPI 635 Charles E. Young Dr. South Room 347 Los Angeles, CA 90095-7332</td>
</tr>
<tr>
<td>Piero Rinaldo, MD PhD Biochemical Genetics Laboratory Department of Laboratory Medicine Mayo Clinic 200 First Street SW Rochester, MN 55905</td>
<td></td>
</tr>
<tr>
<td>Kimberly A. Chapman, MD PhD FACMG Assistant Professor of Pediatrics Section of Genetics and Metabolism Children’s National Medical Center 111 Michigan Avenue, N.W. Washington, D.C. 20010</td>
<td></td>
</tr>
<tr>
<td>Mendel Tuchman, MD Professor of Pediatrics Biochemistry &amp; Molecular Biology Children's National Medical Center 111 Michigan Avenue, N.W. Washington, D.C. 20010-2970</td>
<td></td>
</tr>
<tr>
<td>Carla Curbert, PhD FACMG FCCMG Chief Newborn Screening and Molecular Biology Branch And the Newborn Screening Quality Assurance Program Division of Laboratory Sciences NCEH Centers for Disease Control and Prevention 4770 Buford Highway, MS-F43 Atlanta, GA 30341</td>
<td></td>
</tr>
<tr>
<td>Kelko Ueda, MPH RD LDN Clinical Dietitian Specialist Biochemical Diseases (Metabolism) Program British Columbia Children’s Hospital 4480 Oak Street, K-311 Vancouver, BC V6H 3V4 Canada</td>
<td></td>
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<tr>
<td>Elaina Jurecki, MS RD BioMarin Pharmaceutical Inc. 105 Digital Drive Novato, CA 94949</td>
<td></td>
</tr>
<tr>
<td>Charles P. Venditti MD PhD Genetic Disease Research Branch National Human Genome Research Institute National Institutes of Health Bldg 49, Room 4A56A Bethesda, MD 20892-4472</td>
<td></td>
</tr>
<tr>
<td>Stephen G. Kahler, MD Director, Metabolism Services UK Pediatric Specialty Clinic 740 S. Limestone Second Floor, Wing D, Room J201 Lexington, KY 40506</td>
<td></td>
</tr>
<tr>
<td>Jerry Vockley, MD PhD Professor of Human Genetics &amp; Pediatrics Chief of Medical Genetics Children’s Hospital of Pittsburgh 3705 Fifth Avenue Pittsburgh, PA 15213</td>
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</tr>
</tbody>
</table>

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Fax 866.539.4060
www.oaanews.org

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**Stephanie Carleton and Josh McMahon**
OAA Natural History Registry Coordinators
Financial Report

As is our custom, each year after filing the OAA annual 990 report with the IRS, the board of the OAA publishes the organization’s financial status. The statement shown here details years 2019 and 2020.

Thanks to the generosity of our supporters, we were able to accomplish the following during 2020.

- Hosted table at the Rare Disease Day Event at the University of Minnesota - February 2020
- Mailed over 275 KN95 safety masks in early 2020 to OAA families for COVID-19 protection
- Collaborated with other support groups on a survey on COVID-19 experiences affecting daily lives
- Planning for the OAA Family Conference, but eventually postponed until June 2022
- Started a weekly Zoom Friendship Meet-Up for young adults with an OA disorder
- Published and mailed three newsletters in 2020
- Awarded a $20,000 Grant to the NIH
- Awarded a $500 Grant to the Emory University to their Nutrition Research Program
- OAA participated in Everylife Foundation - Rare on the Road virtual program - June 2020
- OAA spoke at MetabolicUK Virtual Conference - October 2020
- OAA attended virtual NORD Rare Disease Summit - October 2020
- Hosted a Town Hall with our medical team at the NIH in December 2020
- Help recruit MMA and PA families in Hemoshear Insight Study
- Collaborated with Rare Science, Inc. to send Rare Bears to OAA children

<table>
<thead>
<tr>
<th></th>
<th>FY 2020</th>
<th>FY 2019</th>
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<tr>
<td><strong>REVENUE</strong></td>
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<td>Contributions</td>
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<td><strong>FUND CHANGE</strong></td>
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<tr>
<td>(Revenue-Expenses)</td>
<td>$7,518</td>
<td>$22,768</td>
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<td><strong>ENDING FUND</strong></td>
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</tr>
<tr>
<td>BALANCE</td>
<td>$76,237</td>
<td>$68,719</td>
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</table>
A new infographic is available for families of children with cobalamin cofactor metabolism defects (also known as cbl defects) that cause homocystinuria. This infographic describes combined disorders (such as cblC defect) and single disorders (such as cblG defect) and how they can affect the body.

Visit the Organic Acidemia Association website to view or download the infographic! Please see the links below:

**Living with a cobalamin cofactor metabolism defect**
What you should know about cbl defects that cause homocystinuria

[English version](https://tinyurl.com/cvbr9cw)

**Vivir con un defecto en el metabolismo del cofactor cobalamina**
Lo que debe saber sobre los defectos de cobalamina (cbl) que causan la homocistinuria

[Versión en español](https://tinyurl.com/cyteu6vm)

The infographic was provided as an educational resource by Recordati Rare Diseases, Inc. At Recordati, we focus on the few - those affected by rare diseases. They are our top priority and at the core of everything we do. Our mission is to reduce the impact of extremely rare and devastating diseases by providing urgently needed therapies. We work side-by-side with rare disease communities to increase awareness, improve diagnosis and expand availability of treatments for people with rare diseases.
Victor was born on the 8th of June 2019, weighing 3430g and measuring 50cms. At birth, detected beforehand with ultrasound, he had a small VSD (hole in the heart), which later closed over. That ‘minor’ problem became the least of anyone’s concerns, after we were called in to our local hospital on Day 11 for a repeat NBST, as his first one returned an abnormal result. On Day 12 the hospital called us back in again for him to be admitted, breastfeeding was ceased immediately, he was catheterized and put on a drip, then the next day we were flown to Westmead’s Sydney Children’s Hospital, where we received the shock of his diagnosis.

Victor has a rare genetic metabolic condition - Isovaleric Acidemia (IVA). The incidence of IVA in Australia is approximately 1 in 200,000 births. It occurs due to an autosomal recessive gene being passed on to the offspring by both parents. A person with IVA is lacking a particular enzyme needed to break down one of the essential amino acids (leucine) in food. The enzyme defect results in the accumulation of isovaleric acid and other metabolites in the blood and urine which are toxic and harmful to the brain. If left unmanaged, this may lead to the person having a metabolic crisis as well as causing brain damage. The aim of treatment of IVA is to keep the accumulation of isovaleric acid as low as possible by ensuring adequate intake of energy and providing a diet with a moderately decreased protein intake.

We spent 5 days in Westmead where Victor was carefully assessed through daily blood tests. He was started on metabolic formula, Energivit, which he still takes to this day to supplement his diet so that he meets all of his nutritional requirements. By the end of the 5 days I was allowed to recommence breastfeeding which I continued to do for 11 months. 4 months down the track, he was also having some regular supermarket grade formula, as blood tests indicated that he was able to handle, and needed, higher levels of protein in his diet.

At present, he is allowed one high protein (5g) serve per day, with the rest of his daily food intake being of low protein sources which don’t have to be weighed. In addition to this dietary protein restriction, Victor takes 12ml per day of L-Carnitine which helps his body to excrete excess Isovaleryl CoA. We attend clinic with the Metabolic Team at Westmead every 6 months where they monitor his blood amino acids and carnitine levels but since the COVID pandemic began, this clinic is conducted by Telehealth Conference from my home and his bloods are taken from our local pathology centre and sent down to the team at their Westmead surgery.

The danger for him is if he becomes sick with either a high temperature, vomiting or diarrhea, this can lead to him breaking down his own body protein, causing an overload of toxic metabolites. When this happens, the on-call Metabolic Doctor is phoned immediately and Victor’s ‘unwell’ feeding plan is followed where protein intake is restricted even further and calories are increased until he becomes well again and his normal eating patterns return. He has had a couple of respiratory infections in his life with no adverse effects and just one hospitalization when he had vomiting and high temperatures. Once again, our local hospital liaised with the Metabolic Team and they worked closely together to restore Victor’s health. We are so grateful to have the Westmead Metabolic Team managing Victor’s life and know we can contact them at any time with any concerns that may arise as he grows.

Victor’s initial diagnosis came as a shock, as none of our family had ever heard of such a condition. Not to mention, he is my first and only child and I was/still am a single mother. I didn’t break down and cry though, as I felt that would be of no use to Victor. There was no other choice but to accept the hand we had been dealt, learn as much as I could about the condition and try to do my absolute best to take care of him by following the Metabolic Team’s directions and ensuring he gets what he needs, medication-wise and nutritionally.

We also have wonderful family support which I am so grateful for and lucky to have. I cannot imagine our IEM journey without their ongoing love and support – shout out to Mum, Wendy and sister Biggle, who have dropped everything to come to our aid in times of need. To my other sister Vv, for all her help during that...
first 12 months that we were living together. Also to the men, they know who they are.

As for Victor’s special diet it was no adjustment or cause of added stress for me, as I was already eating mostly plant-based well before Victor was on the scene. I am also a huge foodie and love cooking from scratch, so after endless recipe hunting for low protein options and finding the right substitutes for certain ingredients, it is always a pleasure to throw together something delicious for us to both share and enjoy. Mum also grows beautiful veggies, so I am never short of quality organic produce. We also never leave home without a snack pack of yummy home-made Victor-friendly nibblies.

He recently started two days per week of day care to have some added stimulation and socializing. The centre supplies his food and they have been most accommodating of his needs. He eats only low protein foods while there and I save his high protein serve to have at home, where I can monitor how much he has eaten.

At almost 2 years of age, Victor is happy, healthy and unstoppable. He loves his food and play and keeping the family on all of our toes. I couldn’t feel happier or any luckier for all the love, joy and life lessons this little human being has brought and continues to bring to our lives.

Shannon
cricketbrazier@gmail.com
Orange NSW 2800 Australia

HERO Clinical Study Recruiting Participants

The HemoShear Therapeutics HERO (HElp Reduce Organic Acids) clinical study is recruiting participants at leading children’s hospitals across the United States.

The study is enrolling children and adults with MMA (mutase deficient) and PA aged 2 and older who meet the study criteria.

The HERO study will assess the safety, effectiveness and metabolism of HST5040, an oral investigational drug developed by HemoShear to potentially reduce the toxins that cause harm in MMA and PA patients. HST5040 has the potential to be active throughout the body, including the brain, heart, liver, kidneys and muscles.

The investigational drug can be taken conveniently at home as a daily liquid formulation by mouth or through a gastric feeding tube. Study participants will have the opportunity to continue to take the drug until it is approved for use or the study ends.

You can learn more about the study at – MMA-PAHero.com

The safety and effectiveness of HST5040 for the treatment of MMA or PA have not been established.
Hi everyone! My name is Amber Dozier and I have MMA- CblA. My mom has written a few articles about me in previous issues when I was younger, but I thought I would share an update. Recently, I have graduated from Appalachian State University with a bachelor’s degree in Nutrition and Dietetics. My diagnosis has always led me to a love for nutrition and figured I would take it to the next step. In August, I will start graduate school at Appalachian State University for a Master of Science degree in Nutrition and my Dietetic Internship. I am ecstatic to start a new program and see where my interest in nutrition leads me. When not in school or studying, I enjoy taking my dog for a walk, spending time with friends, and painting.

In the past few months, my dietitian and medical team at UNC-Chapel Hill Hospitals have decided I consume enough dietary protein to decrease my intake of Propimex-2 and oral B12. I used to consume 70 grams of Propimex-2 daily, but now I take 50 grams 3-4 days a week. I am still getting used to this dramatic change but it is a lot easier when I travel for vacation to not pack a lot of Propimex-2. I still take my B12 orally 3-4 days a week and try to take it the same days I take Propimex-2. I mix 4oz. of cow’s milk with my Propimex-2 to create a shake-like texture and have adapted to the taste. On top of MMA, I have a severe egg allergy which makes eating difficult. I am thankful for this decrease in my diet but need to ensure I am consuming enough dietary protein to make up for it. As far as dietary protein goes, I shoot for 40-60g a day but do not keep a food record. I do not eat a lot of meat still and never go over my daily protein recommendation. I visit UNC-Chapel Hill Hospitals annually and also get labs taken annually to see how my body is responding to these changes. I am especially thankful for my dietitian, Emily Ramsey, who helped me gain experience in the field and help guide me through my dietary changes!

Please feel free to reach out to me!

Amber Dozier
Greensboro, NC
dozieran@appstate.edu
# New Approaches Being Studied for MMA and PA – Gene Therapy

<table>
<thead>
<tr>
<th>Treatment in Development</th>
<th>hLB-001 by LogicBio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How LogicBio’s Therapy Works</strong></td>
<td>Using a virus (AAV) and a DNA-editing technology, a working copy of the gene is inserted into the patient’s DNA to give cells the instructions they are missing to make needed proteins on their own.</td>
</tr>
<tr>
<td><strong>Disease</strong></td>
<td><strong>MMA MMUT</strong></td>
</tr>
<tr>
<td><strong>Study</strong></td>
<td>SUNRISE Phase 1/2 study assessing two different doses of hLB-001 in patients 6 months to 12 years old. All participants receive the gene therapy. Study is recruiting patients at several sites in the U.S. ClinicalTrials.gov Identifier: NCT04581785</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Patients are infused with one dose of hLB-001 in the hospital and then come to study center multiple times over 12 months to be assessed</td>
</tr>
</tbody>
</table>

# New Approaches Being Studied for MMA and PA – mRNA Therapy

<table>
<thead>
<tr>
<th>Treatment in Development</th>
<th>mRNA-3927 by Moderna</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How mRNA Therapy Works</strong></td>
<td>Messenger RNA (mRNA) is delivered to cells to make the normal functioning protein. Does not insert into DNA of the cell so does not permanently change DNA.</td>
</tr>
<tr>
<td><strong>Disease</strong></td>
<td><strong>PA PCCA/PCCB</strong></td>
</tr>
<tr>
<td><strong>Study</strong></td>
<td>Paramount Phase 1/2 study assessing mRNA-3927 in patients 1 year and older. Participants are grouped to receive the therapy in different doses until optimal dose determined. Study is recruiting patients in the U.S. ClinicalTrials.gov Identifier: NCT04159103</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Patients receive therapy infusion in the hospital for one day every 3 weeks.</td>
</tr>
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</table>
## New Approaches Being Studied for MMA and PA – Oral Therapy

<table>
<thead>
<tr>
<th>Treatment in Development</th>
<th>HST5040 by HemoShear Therapeutics, Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How Oral Therapy Works</strong></td>
<td>HST5040 is a “small molecule” with potential to enter tissues and be active throughout the entire body. This may lead to a reduction in toxins accumulating in the kidneys, liver, heart, muscles and brain.</td>
</tr>
<tr>
<td><strong>Disease</strong></td>
<td>MMA MMUT, CblA, CblB and PA PCCA/PCCB</td>
</tr>
<tr>
<td><strong>Study</strong></td>
<td>HERO Phase 2 study assessing HST5040 in MMA and PA patients 2 years and older. The study is in 3 parts, starting with all patients taking HST5040 in increasing dose levels. Next, patients are grouped to receive either the study drug or placebo for 3 months and then cross over to the other option for another 3 months. Finally, all participants take HST5040 at the optimal dose until the study is complete. Study is recruiting patients in the U.S. ClinicalTrials.gov Identifier: NCT04732429</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Patients take liquid therapy orally or through gastric feeding tube at home daily.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment in Development</th>
<th>BBP-671 by CoA Therapeutics, Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How BBP-671 May Work</strong></td>
<td>BBP-671 is a small molecule (a low weight organic compound) that is designed to activate pantothenate kinases, which are critical for making coenzyme A (CoA). In PA and MMA, defects in PCC and MUT enzymes are thought to result in a shortage of CoA. By increasing CoA, BBP-671 may restore energy to cells, which we believe may help alleviate the enzymatic defects in PA and MMA patients.</td>
</tr>
<tr>
<td><strong>Disease</strong></td>
<td>PA PCCA/PCCB MMA MMUT (± transplant)</td>
</tr>
</tbody>
</table>
| **Study** | CoA Therapeutics is planning a Phase 1 study assessing the safety of BBP-671 in healthy volunteers aged 18 years and to 55 years. ClinicalTrials.gov Identifier: NCT04836494  

CoA Therapeutics is hoping to open the study for MMA and PA patients in the United States later this year. |
| **Administration** | BBP-671 tablets for oral use. |
A message to the PA and MMA community from CoA Therapeutics

At CoA Therapeutics, Inc., an affiliate of BridgeBio Pharma, Inc., we are as committed as ever to moving our program forward to develop our small molecule therapy for patients living with PA and MMA, and other conditions associated with coenzyme A (CoA) deficiency*. We are excited to update you on our recent progress.

We have completed the necessary preclinical studies in animals with our small molecule drug candidate, BBP-671, to support beginning human trials. Additionally, the U.S. Federal Drug Association (FDA) has approved our Investigational New Drug (IND) application to study BBP-671 in humans. In April 2021, we started a Phase 1 study to assess the safety of the drug in healthy volunteers before it is studied in PA and MMA patients. We plan to begin PA and MMA patient trials once we know that the drug candidate is safe, and we have identified a dose appropriate for PA and MMA patients.

We are committed to studying our drug in PA and MMA patients globally. We have been granted Orphan Drug and Rare Pediatric Disease Designations in the United States and we have filed for orphan drug designation in the European Union.

If you would like further information or have any questions, please do not hesitate to contact us at info@coatherapeutics.com.

We know that this continues to be a difficult time for many families, and that current circumstances often pose increased challenges on families caring for patients with PA and MMA. We are committed to advancing our potential therapy for PA and MMA patients as quickly and as safely as possible.

Warm regards,

The CoA Therapeutics Team
LogicBio Therapeutics, Inc. (Nasdaq:LOGC), a clinical-stage genetic medicine company pioneering gene editing and gene delivery platforms to address rare and serious diseases from infancy through adulthood, today announced that the first patient has been dosed with LB-001, the Company’s investigational single-administration gene editing therapy based on its proprietary GeneRide™ platform, in the SUNRISE Phase 1/2 clinical trial in pediatric patients with methylmalonic acidemia (MMA). The child received the intravenous infusion of LB-001 at Monroe Carell Jr. Children’s Hospital at Vanderbilt.

“Today’s landmark announcement represents a significant step forward in gene editing for children suffering from early onset genetic diseases,” said Frederic Chereau, president and chief executive officer of LogicBio. “In addition to dosing the first patient, we have now opened several trial sites and identified enough additional patients to fully enroll SUNRISE, subject to screening clearances. We look forward to providing an update on enrollment, dose escalation and age de-escalation in late 2021. In addition, we continue to expect to announce interim clinical data by the end of the year.”

“This moment represents the next step in a potential new era for the treatment of MMA,” said Kathy Stagni, executive director of the Organic Acidemia Association (OAA). “The OAA community of patients and caregivers are grateful to the researchers at LogicBio who have been dedicated to advancing this promising research and it is exciting to see that we are one step closer to a more hopeful future.”

“This moment represents the next step in a potential new era for the treatment of MMA” said Kathy Stagni, executive director of the Organic Acidemia Association (OAA)

MMA is a rare and life-threatening genetic disorder for which there are currently no treatments addressing the underlying cause of the disease. To manage the symptoms and detrimental effects of MMA, patients must maintain a severely restrictive diet. Even with aggressive management, MMA patients often experience metabolic crises that can cause permanent neurocognitive damage.

The SUNRISE trial is initially enrolling patients 3-12 years old and will potentially enroll infants as young as 6 months once the first two patients meet certain safety parameters and a biomarker indicating genome integration and protein expression is detected.

“Many genetic medicines are unable to target pediatric indications such as MMA, but an early and durable intervention in this vulnerable population has the potential to prevent disease progression and irreversible symptoms, including neurological damage,” said Daniel Gruskin, MD, chief medical officer of LogicBio. “Our goal is to provide a safe and durable therapeutic option to treat MMA early enough to make a meaningful difference in patients’ lives and eliminate the need for invasive liver transplantation, which is increasingly performed in children suffering from this disease.”

“This milestone takes us one step closer to bringing a much-needed treatment option to patients living with MMA. I look forward to helping advance the SUNRISE trial and seeing the results,” said Thomas M. Morgan, MD, the principal investigator of the SUNRISE trial at Monroe Carell Jr. Children’s Hospital at Vanderbilt.

About the SUNRISE Trial

The SUNRISE trial is an open-label, multi-center, Phase 1/2 clinical trial designed to assess the safety and tolerability of a single intravenous infusion of LB-001 in pediatric patients with methylmalonic acidemia (MMA) characterized by methylmalonyl-CoA mutase gene (MMUT) mutations. On June 2, 2021, the Company announced that the first patient was dosed. Seven leading centers in the United States and one in Saudi Arabia are expected to participate in the trial. With the aim of evaluating LB-001 at an early age, before irreversible damage has occurred, the SUNRISE trial is initially enrolling 3-12 year old patients with the potential...
to include infants as young as 6 months old after meeting certain safety parameters and biomarker detection. The SUNRISE trial will enroll up to 8 patients and evaluate a single administration of LB-001 at two dose levels.

**About LB-001**

LB-001 is an investigational, first-in-class, single-administration, gene editing therapy for early intervention in methylmalonic acidemia (MMA) using the GeneRide™ platform. GeneRide™ technology utilizes a natural DNA repair process called homologous recombination that enables precise editing of the genome without the need for exogenous nucleases and promoters that are associated with an increased risk of immune response and cancer.

LB-001 is designed to non-disruptively insert a corrective copy of the methylmalonyl-CoA mutase (MMUT) gene into the albumin locus to drive lifelong therapeutic levels of MMUT expression in the liver, the main site of MMUT expression and activity. LB-001 is delivered to hepatocytes via livertargeted, engineered recombinant adeno-associated virus vector (rAAV-LK03). Preclinical studies found that LB-001 was safe and demonstrated transduction of hepatocytes in a mouse model of MMA demonstrated preferential survival and expansion (selective advantage), thus contributing to a progressive increase in hepatic MMUT expression over time. LB-001 resulted in improved growth, metabolic stability, and survival in MMA mice. The U.S. Food and Drug Administration (FDA) granted Fast Track designation for LB-001 for the treatment of MMA. In addition, the Company has received rare pediatric disease designation and orphan drug designation from the FDA for LB-001.

**About Methylmalonic Acidemia (MMA)**

Methylmalonic acidemia (MMA) is a rare and life-threatening genetic disorder affecting approximately 1 in 50,000 newborns. In the most common form of MMA, a mutation in a gene called methylmalonyl-CoA mutase (MMUT) prevents the body from properly processing certain fats and proteins. As a result, toxic metabolites accumulate in the liver, in muscle tissue and in the brain. Symptoms include vomiting, lethargy, seizures, developmental delays and organ damage. There is no approved medical therapy addressing the underlying cause of the disease. To manage the symptoms, patients go on a severely restrictive, low-protein, high-calorie diet, often through a feeding tube. Even with aggressive management, these patients often experience life-threatening metabolic crises that can cause permanent neurocognitive damage. Because of the need for early intervention, newborns are screened for MMA in every state in the United States.

**About LogicBio Therapeutics**

LogicBio Therapeutics is a clinical-stage genetic medicine company pioneering gene editing and gene delivery platforms to address rare and serious diseases from infancy through adulthood. The Company’s first platform, GeneRide™, is a new approach to precise gene insertion harnessing a cell’s natural DNA repair process potentially leading to durable therapeutic protein expression levels. The Company’s second platform, sAAVy™, is an adeno-associated virus (AAV) capsid engineering platform designed to optimize gene delivery for treatments in a broad range of indications and tissues. The Company is based in Lexington, MA.

For more information, visit [www.logicbio.com](http://www.logicbio.com), which does not form a part of this release.
Researchers at the National Institutes of Health have developed a breath test that measures how well patients with methylmalonic acidemia (MMA) respond to receiving liver or combined liver and kidney transplantation. Researchers also used the test to assess the severity of the disease in people and help determine if they would benefit from surgical or experimental genomic therapies that target the liver. The study results were published in Genetics in Medicine. Scientists at the National Human Genome Research Institute (NHGRI) led the project team, with collaborators from the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute of Mental Health.

MMA is a rare genomic disease that impairs the body’s ability to metabolize certain proteins and fats. This causes toxic substances to build up, which may result in kidney disease, pancreatitis, movement disorders, intellectual impairments, complications in many organs, and, in severe cases, death. One in 80,000 children born in the United States are diagnosed with MMA during newborn screenings. Currently, MMA is incurable, but people with MMA manage their symptoms through dietary restrictions and vitamin supplements. In extreme cases, patients receive liver or combined liver and kidney transplants, which help restore normal levels of metabolic proteins.

“Vast fluctuations in metabolic substances in the bodies of patients make it difficult for us to tell if treatments like genome editing and transplants are likely to be successful,” said Charles P. Venditti, M.D., Ph.D., senior author and senior investigator in the NHGRI Medical Genomics and Metabolic Genetics Branch. “Instead of looking at levels, we decided to measure metabolism itself.”

One form of MMA is caused by mutations in the methylmalonyl-CoA mutase gene (MMUT), which encodes for the MMUT protein. People with this form of MMA have a deficiency in the MMUT protein, which plays a pivotal part in metabolism. The protein is involved in the biological steps that help break down food, fats, cholesterol and amino acids.

MMUT helps break down food into a chemical byproduct called propionate, which is followed by an integral process involved in metabolism called oxidation. Through oxidation, a healthy body converts propionate into energy and carbon dioxide, which is exhaled, but that process is faulty for people with MMA.

Because MMUT protein function is compromised in people with MMA, Venditti and his team chose to assess how well the MMUT protein helped break down propionate in both patients who did and did not receive treatment. The researchers believed this would act as a proxy for how much oxidation was happening in a patient’s body.

“We wanted to measure exhaled carbon dioxide because we planned to use a breath test to track oxidation of propionate in a non-invasive way,” said Irini Manoli, M.D., Ph.D., co-author and associate investigator in the NHGRI Medical Genomics and Metabolic Genetics Branch.

“The trick was to somehow ‘mark’ the carbon dioxide so we could see which patients are unable to oxidize propionate because of a faulty MMUT protein.”

Usually, the carbon dioxide we exhale as a result of propionate breaking down in the body contains a lighter, more common form of carbon, carbon 12. But because carbon dioxide that contains carbon 12 is released by several metabolic processes in the human body, simply measuring carbon dioxide exhaled by MMA patients would not show how well MMUT helped oxidize propionate. To
detect if the MMUT protein was functioning properly, researchers gave patients a dose of the heavier, less abundant version of carbon — carbon 13 — via a commercially available food additive. The team recruited 57 study participants, including 19 MMA patients who had received transplants (liver, kidney or both) and 16 healthy volunteers. Researchers gave participants a dose of the food additive containing carbon 13 via a drink or through a feeding tube, and then collected their breath samples after a two-minute wait.

The researchers measured how much of the exhaled carbon dioxide contained the usual carbon 12 compared to added carbon 13. As hypothesized, MMA patients who did not receive any treatment had lower levels of carbon 13 than healthy volunteers. By contrast, MMA patients with liver transplants had higher levels of carbon 13, similar to the healthy volunteers. This result indicated that the MMUT protein was helping oxidize the carbon 13 molecules by bonding with inhaled oxygen molecules. Higher levels of carbon 13 oxidation also correlated with better clinical outcomes, such as improved cognition and slower decline in kidney function.

Currently, the test is only available for use at the NIH Clinical Center; however, the researchers hope it will soon be broadly adopted for clinical and research use.

“Our next goal is to see if this specialized breath test can detect increase in carbon 13 propionate oxidation after gene, mRNA or genome editing therapies,” Venditti said. “This way, we can also use this test to measure how effective these treatments are in restoring MMUT function.”

NHGRI is one of the 27 institutes and centers at the National Institutes of Health. The NHGRI Extramural Research Program supports grants for research, and training and career development at sites nationwide. Additional information about NHGRI can be found at https://www.genome.gov.

About the National Institutes of Health (NIH):

NIH, the nation’s medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

References


Loprofin pastas are low protein foods for the dietary management of inborn errors of metabolism and other conditions requiring a low protein diet and must be used under medical supervision.

Brought to you by Nutricia North America
Be the OAA Voice in New England!

The New England Connection for PKU and Allied Disorders (NECPAD) is a non-profit organization that supports the OAA community in the six New England states, in the United States of America - Massachusetts, Connecticut, Rhode Island, Vermont, New Hampshire and Maine. NECPAD’s mission includes offering support, organizing social events, providing financial assistance, and advocating on behalf of the patients and families that NECPAD proudly serves. Currently NECPAD is looking for a volunteer OAA representative to join its’ Board. Duties would include, but are not limited to, attending a virtual meeting one evening a month, and acting as a liaison between NECPAD and OAA patients, care providers and families. To inquire, please email necpad.org@gmail.org. To find out more about NECPAD visit necpad.org.

HCU Network America, Organic Acidemia Association, Propionic Acidemia Foundation | 2022 Conference

LAND OF THE FREE, HOME OF THE BRAVE

June 25-26, 2022 | Bethesda, Maryland

Save the Date
The research team at HemoShear Therapeutics would like to better understand what day-to-day life is like with methylmalonic acidemia (MMA) or propionic acidemia (PA).

The company is looking to conduct a series of one-hour interviews (by phone or Zoom) to hear about your experience. The more we learn from you, the more we can represent the patient and family perspectives when developing and evaluating potential new treatments.

If you are a person with MMA or PA or a caregiver (parent, partner, family member), you may qualify to participate in our upcoming interview study. Both transplant and non-transplant recipients are eligible.

The interviews will be conducted by an outside company specializing in researching patient disease experiences, and no personally identifying information will be provided to HemoShear.

For additional information or if you want to share your experience to help develop new treatments, please e-mail MMAandPA@endpointoutcomes.com.
Driven by our mission to deliver on the promise of mRNA science to create a new generation of transformative medicines for patients, Moderna recognizes the impact of rare diseases on patients and their families, particularly when the disease lacks any effective treatment options.

We remain committed to advancing mRNA-based therapeutics in Propionic Acidemia (PA) and Methylmalonic Acidemia (MMA), and we are pleased to share that our first program in PA is open to enrollment in the US, Canada, and the UK. We also expect our MMA study to commence in 2021.

The Paramount Study is a Phase 1/2 study. It is designed to evaluate if an investigational treatment called mRNA-3927 is safe in individuals one year of age and older with PA. mRNA-3927 is an investigational intravenous (IV) infusion treatment that instructs a persons’ body to make a PCC enzyme that works.

More information including full trial inclusion and exclusion criteria can be found at Moderna Paramount Study or by visiting ClinicalTrials.gov

The Landmark Study is a Phase 1/2 study. It is designed to evaluate if an investigational treatment called mRNA-3705 is safe in individuals one year of age and older with MMA. mRNA-3705 is an investigational intravenous (IV) infusion treatment that instructs a persons’ body to make a MUT enzyme that works.

More information including full trial inclusion and exclusion criteria can be found at Moderna Landmark Study or by visiting ClinicalTrials.gov
Easy-to-Understand MMA/PA Education for New Families

TEMPLE (Tools Enabling Metabolic Parents Learning) from Nutricia North America is an educational series for inborn errors of metabolism, including Glutaric Aciduria Type 1 (GA-1), Isovaleric Acidemia (IVA), Methylmalonic/Propionic Acidemia (MMA/PA), and others.

These booklets and videos explain the condition and its management in easy-to-understand language and pictures. They are ideal for educating new parents and families after a positive newborn screening.

Nutricia is proud to now offer a TEMPLE booklet for MMA/PA!

Browse and download this introductory educational booklet on Nutricia’s website: medicalfood.com/learning-center/

(Click on “Educational Tools” and scroll to various disorder-specific resources.)

NEW Organic Acidemia Education in Arabic!

Nutricia North America strives to support all members of the Organic Acidemia Association.

Nutricia’s basic educational booklet series called TEMPLE is now available in Arabic! TEMPLE education is also available in English, Spanish, and French.

Share and access these introductory educational booklets on Nutricia’s website: medicalfood.com/learning-center/

(Click on “Educational Tools” and scroll to various disorder-specific resources.)
Organic Acidemia Association

(OAA) provides information and support to parents and professionals dealing with a set of inborn errors of metabolism collectively called organic acidemias. The OAA is a volunteer organization registered with the IRS as a 501(c)(3) non-profit corporation. Donations to the OAA are tax deductible. OAA publishes a newsletter three times a year, hosts a Google Group for information exchange and maintains a website and Facebook page. Services are funded by corporate and individual donations. Annual membership donation of $25 (US) and $35 (international) plus $5 for the family roster is requested, but not required. Our 501(c)(3) non-profit status qualifies OAA for United Way donations through their write-in option. If there is a write-in option, just write “Organic Acidemia Association” in the blank line on your pledge card.

Donations can also be made at OAA’s website through the “PayPal” and the “Network for Good” option.

- The information contained herein does not necessarily represent the opinions of our Board of Medical Advisors or Board of Directors
- Letters and photographs sent to OAA become the property of OAA and may be used or edited at the discretion of the OAA staff.
- Names or information will be kept confidential only if specifically requested in writing
- This newsletter does not provide medical advice. You should notify your health care provider before making treatment changes.

ANNUAL DONATION / CHANGE OF ADDRESS

Please accept $___________ as our annual tax deductible donation to the Organic Acidemia Association.

Suggested membership donation is $25 (US) and $35 (international). Extra funds are welcome and can be designated for research, OAA operating expenses, or to help others attend conferences.

Remember the newsletter does not get forwarded when you move!

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