Spring is always an exciting time of year as the sun moves higher in the sky, temperatures warm, and trees and flowers bloom. In some ways we are also in the “spring” of SMA research. Groundwork undertaken by us and our colleagues at other institutions has established an effective network of centers ready to share our strengths. Furthermore, research in basic science laboratories has provided seeds of knowledge that we hope will now grow and blossom into effective treatments in human trials.

With that in mind, we are happy to announce that in May we will start a Phase I clinical trial using a compound known as ISIS 396443 or ISIS-SMNRx. Not exactly a “drug,” this compound is a small piece of DNA that will be injected into a patient’s spinal canal. The Phase I trial is designed to look at the safety of this compound in humans, at how well it is tolerated, to assess signs of efficacy, and to determine what the best dosage will be.

In animal experiments, ISIS-SMNRx increased the production of SMN protein in the motor neuron cells of the spinal cord. Our hope is that humans who are given ISIS-SMNRx will also see increased SMN protein and that it will lead to improved motor function. Overall, this spring we are optimistic that we are getting closer and closer to an effective treatment or cure for this disease.

**From the Desk of Dr. Darras:**

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**CLINICAL STUDY OF ISIS-SMNRx**

Children’s Hospital Boston is proud to be a part of a Phase I trial for a new SMA drug. This study is testing the safety and tolerability of ISIS-SMNRx, a drug that may be a potential treatment for all Types of SMA. The ISIS-SMNRx drug was developed by Isis Pharmaceuticals, Inc., a company in California that uses antisense technology to discover and develop novel drugs for a wide variety of diseases.

ISIS-SMNRx is designed to treat SMA by altering the splicing of the SMN2 gene that leads to the increased production of fully functional SMN protein. This approach has been thoroughly validated in animal models, using both mice and monkeys. These studies have shown that the drug can successfully alter the disease course in both mild and severe models of SMA.

“A disease-modifying drug like ISIS-SMNRx that specifically targets the cause of the disease could, for the first time, restore muscle strength and respiratory function and dramatically improve the children’s function and quality of life,” said Darryl C. DeVivo, M.D, Sidney Carter Professor of Neurology and Pediatrics and Co-Director of the Motor Neuron Center at Columbia University Medical Center.

The Phase 1 study of ISIS-SMNRx is a single-dose study designed to assess the safety, tolerability and pharmacokinetic profile of this drug in children with SMA. This is a dose-escalating study, so we will evaluate several different doses of the drug. Children with types II and III SMA, who are between the ages of 2 and 14, and who are medically stable, are eligible for this trial. A total of 24 children will be involved, and we
Meet the SMA Team:

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<tr>
<th>Neurology</th>
<th>Orthopaedics</th>
<th>Pulmonary</th>
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<tr>
<td>Dr. Basil T. Darras</td>
<td>Dr. Frederic Shapiro</td>
<td>Dr. Robert Graham</td>
</tr>
<tr>
<td>Director, NM Program, Principal Investigator</td>
<td>Attending Physician</td>
<td>Intensivist / Home Care</td>
</tr>
<tr>
<td>Dr. Peter Kang</td>
<td>Rebecca Parad</td>
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</tr>
<tr>
<td>Attending Neurologist, EMG Specialist</td>
<td>Clinical Coordinator</td>
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<td>Dr. Jennifer Markowitz</td>
<td>Kerri Shaw</td>
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<tr>
<td>Attending Neurologist</td>
<td>Admin. Assistant</td>
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Meet the extended SMA Team:

While our Neuromuscular Clinic is multidisciplinary and includes many amazing people, we realized that SMA care extends into other disciplines. To alleviate confusion and enhance communication we have established an amazing team of people in various specialties that work closely with many families with SMA and are willing to work together with us to provide the best care as possible to patients. While these individuals are not directly part of our multi-disciplinary clinic, we hope that may change in the future to minimize the number of medical visits families have to attend.

We understand that some families affected by SMA have found other health care providers who are not on the list below very helpful. We encourage families to stay with those providers as this list is not exhaustive. In addition to helping families directly, these individuals have offered amazing support to their colleagues working with patients with SMA.

For purposes of saving space, full titles and contact information is not available here. However, if you would like to get in touch with one of these specialists, or any other at Children’s Hospital Boston, about making an appointment, please contact Gretchen DeLuke or Beth Shriber.

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<tr>
<th>Pulmonary</th>
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<th>PACT Team</th>
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<tr>
<td>Dr. Virginia Kharasch</td>
<td>Dr. Laurie Fishman</td>
<td>Dr. Joanne Wolfe</td>
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<td>Social Work</td>
<td>Anesthesiology</td>
<td>Dr. Tamara Vesel</td>
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<tr>
<td>Shuei Kozu, LICSW</td>
<td>Dr. Navil Sethna, Dr. Chuck Berde</td>
<td>Dr. Christy Ulrich</td>
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<tr>
<td>Complex Care Service</td>
<td>Surgery (non-orthopedic)</td>
<td>Janet Duncan, Nurse Practitioner</td>
</tr>
<tr>
<td>Dr. Laurie Glader</td>
<td>Dr. Craig Lillehei</td>
<td>Marsha Joselow, Social Worker</td>
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</table>

Meet the extended SMA Team:

Please help us welcome Rebecca Parad to our SMA Team. Rebecca joined us as a Clinical Research Coordinator in July ’11 and will help with all of the research studies detailed here.

Rebecca received a degree in Molecular Biology and Biochemistry from Wesleyan University. She has previous experience working in clinical research at Children’s Hospital Boston and Brigham and Women’s Hospital.

We are very excited to have Rebecca on our team, and we hope that you will introduce yourself to her during your next visit.

Kids’ Corner Answers (questions on page 4):
1) A Sponge
2) A Flag
3) SWIMS

ISIS, continued

hope to recruit around 6 patients here at Children’s Hospital Boston. In this study, ISIS- SMNRx will be administered during a lumbar puncture, as a single injection directly into the spinal fluid. We will then look at cerebral spinal fluid, blood samples, and physical therapy assessments to see how patients respond to the drug.

Children’s Hospital Boston is among several sites participating in this trial. Columbia University Medical Center, UT Southwestern Medical Center and University of Utah School of Medicine are also involved. With all of our combined efforts, we are well on our way to finding a cure for SMA.
Research Updates:

PNCR Natural History Study

We continue our successful collaboration with Columbia University and the Children’s Hospital of Philadelphia in the PNCR Network for Clinical Trials on SMA.

We have been very successful in gathering important information through our natural history study. Nearly one hundred and twenty SMA affected individuals participated in our original study across the three sites. The data collected as part of this study has been highly requested by many groups working on SMA and we are thrilled to be able to provide information that moves research forward.

Going forward, we continue to collect a shortened natural history data set on patients seen in the SMA clinic. This study, also known as the minimal dataset, includes collecting medical history information, along with a short physical therapy exam. Patients are followed for 3 years, having visits whenever they come to clinic. We currently have 21 patients participating in this modified study and hope to enroll around 40 total.

Biomaterials Study:

As part of the PNCR Network, we are involved in a study which aims to create an SMA specimen bank. The primary purpose of this study is to evaluate tissue, blood, urine, and cheek cell samples, which will allow researchers to better understand SMA.

Skin and muscle samples will be collected while patients undergo surgery for clinical reasons. Blood, urine, skin, and cheek cell samples will be collected during SMA clinic visits. These samples will be helpful for researchers to learn more about muscle weakness in patients with SMA, as compared to patients with other neuromuscular disorders and healthy controls.

Currently 48 children and adults have volunteered for this study here at Children’s Hospital Boston, providing us with around 80 samples.

This study is conducted in conjunction with Columbia University in New York and Children’s Hospital of Philadelphia.

NeuroNEXT

Children’s Hospital Boston is proud to have been selected to be part of the National Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT). This network, created by the US National Institute for Neurological Disorders and Stroke (NINDS), aims to facilitate the progress of new drugs from the laboratory to the clinic. Twenty-five clinical centers across the country are involved, creating a wide network of researchers with unique expertise and their patients.

The first NeuroNEXT study will be an investigation of potential biomarkers in SMA. This will focus on newly diagnosed infants, a population of SMA patients that is often overlooked in research. Future studies can be in any area of neurology and can be either observational or drug studies. The network’s aim is to complete at least five studies over the initial seven year period.

NeuroNEXT hopes to relieve some of the roadblocks currently hindering the development of new drugs for neurological disorders. This initiative could greatly benefit researchers, and subsequently patients, through the resulting collaboration.
Upcoming Events:

12th Annual New England Chapter Cure SMA Walk-n-Roll
May 19, 2012 Wompatuck State Park
204 Union St Hingham, MA

This great family event has been raising money for SMA research for over a decade! Take part in a 1.5 mile walk through scenic Wompatuck State Park. Refreshments, children’s games, and entertainment will be provided. Contact Silvia Murphy at silvia@fsma.org for additional details.

2012 Annual SMA Conference
June 21–June 24, 2012
DoubleTree Hotel—Minneapolis South
Minneapolis, MN

Join Families of SMA’s annual conference, which will include networking opportunities, workshops, research updates, and kids’ programs. The hotel is centrally located near the Mall of America, and shuttle buses will be provided for your convenience. Please email info@fsma.org with any questions.

Muscular Dystrophy Association’s Boston Telethon Lock-Up
August 1, 2012

In this jail-themed fundraiser, community and business leaders raise funds to send children to MDA’s summer camp. Participants, or “Jailbirds”, go to the “MDA Jail”, where they are sentenced to one hour of networking and fundraising. Please contact bostonnorth@mdausa.org for details.

The New England area SMA Community is very fortunate to have such a visible and available Families of SMA Chapter. The SMA Team at Children’s Hospital Boston is in constant contact with the board of the New England Chapter, and we would like to reinforce to the families we have contact with what a valuable resource this group is. Not only does the New England chapter do amazing fundraising work, but they are also very passionate about supporting families like their own. If you would like to speak with a member of the New England chapter, please contact newengland@fmsa.org or simply mention your interest to Rebecca or Beth at CHB, Rebecca.Parad@childrens.harvard.edu or Elizabeth.Shriber@childrens.harvard.edu.

Just For Kids

Hey kids! How smart are you? Can you figure out these fun brainteasers?

(Answers on page 2)

#1 What is full of holes but still holds water?

#2 What flies around all day but never goes anywhere?

#3 What word looks the same upside down and backwards?

Word Fun...
Spring is in the air! Can you find these spring flowers?

Rose
Tulip
Daffodil
Peony
Lily
Pansy
Iris
Crocus
Lilac

D O F G O S R E T R
R D J E S X O A I R
I E S E X F S J R L
T Y M E O U E M I I
U I N J C W B L S L
L I D O F F A D G Y
I F R R E C W I O N
P C W S A P A N S Y
X H K M T E T T Q L
E N M W O N I M K N