Tennessee Rare Disease Advisory Committee (RDAC)

Minutes October 27th, 2021

RDAC Members In Attendance:

Other Attendees:

Agenda Item	Notes	Action Item(s)
Call to order and Welcome	Scott Strome, RDAC Chair	
Rare Disease Patient Perspective	Kim Stephens, RDAC Member Lysosomal storage disease deficiency of iduronate-2-sulfatase ⅓ have attenuated form without cognitive regression Diagnosed at age 2-3 or later, usually first sign is ear infection Hernia repair at 6 mos, 500 children in the US, X-linked so boys 2000 worldwide, and only 2 are girls Austin, TX nobody picked it up, moved to TN to ETCH and met Dr. Little who had had a patient with Hunter, and then realized he had the appearance and symptoms. Sent to UT for an adult geneticist, got the Hunter dx. Handed dx and said good luck. Researched it - specialist was 5 hours away at UNC. Saw him every 6 months, had an intrathecal trial into the brain to give the enzyme, but it was on hold, waited 2 years to get into the intrathecal trial. Had a 4 hour treatment by IV infusion, had urgent aortic valve surgery done by David Bichell. ETCH agreed to be a site for intrathecal trial to dose it locally. Gets LP each month, and three other patients came on in COVID because ETCH had a good protocol. Has been in that trial for 6 years but that is another story - picked cognitive outcome measures that were unattainable for boys with Hunter syndrome. Now does work to make outcome measures achievable so these trials will be successful. Cole has had 89 doses of intrathecal. Elaprase is FDA approved and is standard of care. Approved in 77 countries. Costs 330K per year in US. Weekly infusion. Need more by weight. No generic drug. Other treatments. Takeda intrathecal trial extension study. Denali enzyme replacement may cross brain barrier started in 2020. At least 30 boys enrolled in that one. JCR drug is also going to be one of those that crosses the BBB. Should start in Jan. Current ERT doesnt cross BBB. Gene therapy trial going on now, good outcomes with REGENEXBio. Treating older kids, open for over 5yo, treated a boy at 14yo. New lentiviral gene therapy Avrobio, and Sigilon, capsules injected into the liver and secretes the enzyme. When was thinking about Strome's questions. Boys with severe form do not live past age 15. Not enough coverage for speech therapy not enough peds and behaviorists in east tn. Not enough pediatric neurologists in east tn.	

	Toileting assay **Losing skills** **Gene therapy** **National problem gettign neurology spots, filling slots** **Six clinical trials that people can enroll in, how do you fill those slots with a super rare disorder** **Clinical trials need to be accessible to everyone** **If you have options, you have to make a decision as a parent, can be really hard to work with. Is gene therapy the best? Trips to California for 5 years in a row. For the other trials, on site for 6 months to relocate to Pittsburgh or California for 6 months. Start thinking about clinical trials in a different way. Folllow up in telehealth, local draw, video reporting. Same MRI machine, same doctors to compare them, is that really necessary. Challenge the requirements to make it more accessible.**	
Emerging Therapies in Rare Disease	**Marshall Summar, MD, Children's National** **Rare Disease as a Unique Field of Medicine** **True Tennessean, Vanderbilt 1985 to 2010 at Vanderbilt** **Works with VA RDAC too** **8-10% of pop have rare disease, 3-5% very serious** **1:1618 incidence (less than 200K in the US) definition** **Europe 1:2000, Taiwan 1:10,000** **Disease uncommon enough that a GP wouldn't know how to treat it. Since human genome it is now 9000 rare diseases 492 new disease, 9 new diseases per week. Unlike surgeon, in genetics you have to use informatics aggressively. ICD10 has 500 specific rare diseaes codes. ICD11 has xxx codes for rare diseases. ICD has given up on how to keep up. Finding them in EMR is difficult. We have 600 therapies. Survival of patients, are going up. Death rates in spain, life expectancy is going up, rare diseases are now chronic diseases. Coordination of standards and treatment protocols. Patients are surviving, impacts policy decisions.** **Policy, not enough data.** **Outcome data is vairable, genetics are variable.** **NORD board chair for many years.** **Patients are the best source of info - we need to listen to families more.** **Uses more specialities than any other area. Care expertise is limited. Fewere than 5-600 practicing physicians. And fewer than 100. Geneticists.** **Common disease are breaking down into rare diseae clusters. Breast cancer, 30 molecular subtypes, for example. Precision medicine** **Divides more conditions** **34% of peds hosp patients had rare condition** **51% nthe billing** **81% had** **Patients with rare disease code had 12% of visitis outpatient** **18% of inpatient visits were rare diseases** **32% of more than one visit to hosp** **Median cost per year for treating patient is 6-7x non-orphan drugs** **Studies are burdensome** **Orphan drug approvals, act 1983 very successful, 40-50% of new drugs each year, 730 orphan indications,** **Most of these drugs go to oncology, half of orphan drugs** **Metabolism, neurology, infectious disease are next.**	**Put slides on website**

	18-20 of WW drug sales are going forward as orphan inidcations **New and growing therapies, organ transplants, biochemical disorders** **Enzyme replacement, small molecule, substrate and product manipulation, alternate enzymology, mRNA manipulation, gene therapy, gene correction, dietary manipulation** **Under skin in omentum, messenger RNA manipulation, messenger RNA back to patient. Some effective gene therapies, SMA. Wont fix every disease. Modified CRISPR, will see an explosion in technologies.** **Patients on medicaid is a tough nut to crack on dietary manipulations** **There are 289 gene therapies and over 500 listed in FDA, starting to compete for patients. Long-term commitment.** **Adenovisurs discarded, now Adeno-associated virus coming on. Now doing lipid envelope delivery. Magic Bullet to give DNA. Immune issue around it. Fourth death in clin trial. Not a magic bullet.In the eye is good - brain doesn't get geat distribution.** **Viral vector - some looking at herpes and measles virus. DNA delivery. Different viruses target different body parts. If patient has immunity to one can select another. Immune modulation necessary can have long term consequences.** **Important because get one shot with each AAV type. Control arms are problematic. Small molecule first, RNA second, gene therapy third.** **Famileis are stacking the trials. Can't do a cross over and can't do a control. If expose parent can affect future children!!! May wear off over time, in liver for example after 1-2 decades. Not the same problem neuronally.** **Most geneticists are in** **Can use telemedicine, several 100 visits** **Last year, experiment. Telemedicine shortened wait times to a few days. Address simple issues quickly. Decisions quicker, adjustments faster. Saw a lot of benefits for autism, behavior issues, got to see patients in home environment. Dieticians for biochem program could go into the fridge and change the menu plans! Increase frequency of visits. Removes barriers to care. Transportation issues. Singel parent households big burden to come in in person. Balance now is about 60:40 can bring in specialists into the appt. In TN very important because of spread, clinics in Ghana with cell phones.** **Lots of new stuff on visual and facial recognition Downs, Williams, DiGeorge. We need to have PCPs involved earlier. We need them to have the tools in the hands of community providers. Many are interested in complex patients, partner with them. Home testing also very important. Use of buccal swabs for whole genome testing. Can do it at home. Home tests for Phenyl Alanine, ammonia, shortens decision loops. Lot os people say we dont' have enough but** **OMB put one trillion dollars** **Build a new model on clinical genetics for rare diseaes** **ABLE Act** **ACe Kids act** **OMB has resisted making predictions for rare disease** **Costs - life span of 15 years, 5 million cost, gene therapy at 2 million for gene therapy. If you dont' have gene therapy, you hae a lot of other costs carpal tunnel, port infections, added into the price.** **Gene therapy costs are liekly to be less, it is area under the curve.But overall costs, most data comes from hemophilila world. If you can get a long-term fix. Cost savings not included. Payers are interested. Want it done at speciality centers. NROD is sponsoring a centr of excellence program announcement is Nov 4th. Recombinant committee - need to get the genes to express.**	

	Rare disease tax cut. Is incentive program. **Get coverage for supplements and food.** **Keep networking going between centers and groups - what is important for families.** **Cross state licensure is necessary.** **National licensure for rare specialists.** **TN could help MS, Memphis, Get best provider to patient.** **Pressure coming anyway to speed diagnostics with WGS.** **Commercial sequencing providers will take over - cost is low enough to get standardization. Networking of genetic centers will help a lot.** **Out of pocket just keep up with it**	
Annual Report Development ***Update***	**Terry Jo Bichell, RDAC Vice-chair - Please table for today.** **GIllian Hooker, RDAC Member**	
TN Expanded Genomic Diagnostics Program update / TN Rare and Undiagnosed Disease Network ***Update***	**Rizwan Hamid, RDAC Member** **Scott Strome, RDAC Chair** **Chip Chambers, RDAC Member** **Terry Jo Bichell, RDAC Vice-chair** **Rizwan updating: Ashley McMInn is project manager and Dan Harder. We decided to come up with a framework of what the TN Rare Disease Board would look like, what its functions are, and purpose. If we do it and put it into practice we can then seek permanency. Rizwan drafting straw man document. Connecting with UT folks and Chester Brown, drafting document in next 2-3 weeks to circulate. Ashley and Dan need that draft document, to see from a project manager point of view, to say what to do next. Document will be ready in 2 weeks. Working group meeting is today. Can discuss further today. Would be good to have a live meeting of the group at some point, maybe in Nashville. Would be nice to meet in person. Will talk to Jeff Balser about UT and Vandy hosting.**	
Upcoming Meeting Schedule	**Gillian Hooker, RDAC Member, requesting to table this item for today.**	
Brief Updates **Term Limits / Succession** **Pharmacy Advisory Committee Update** **DUR Update** **Newborn Screening / Genetics Advisory Committee Updates**	**Terry Jo Bichell, RDAC Members** **Lora, Scott submitted to gov nomination committee, need new peson from St. Jude's to be nominated asap. Will get ahead in summer.** **Reginald French, RDAC Member** **Lora Underwood, RDAC Member** **PAC meeting is Nov 10 falls on a Wed, Then in Feb.** **Agenda will be up very soon and should be circulated to all of board. As new drugs are developed and FDA approved, they drop into the database, then TennCare develops criteria and then takes them to PAC within next month's meeting and that is when they go to PAC to be reviewed. Place where RDAC would have a place is when RDAC has a place to provide criteria to PAC. At that point RDAC would be important.** **Megan Crow, RDAC Member** **DUR meeting, Katie Beckett 1000 people in program.** **American Rescue Plan act, 3 billion dollars, financial stimulus accountability group, Tenn Care submitted a proposal.**	

Department of Intellectual and Developmental Disabilities **TN Rare Disease Survey**	**Did discuss barriers to pharmacists dispensing 3 day emergency supplies of medications. 10yo study in Texas. TN claims denied for nutritional agents in 7000 cases? Denying very expensive medications for 3-day. Taramadol use in peds, that TennCARE says is not approved for peds due to resp depression, going down the list of ideas on how to make it safer for kids.** **Missed a few sentences.** **Criteria should be updated and passed recommendation to PAC.** **New rec for next month's meeting. What about the 3 billion could we in rare disease be weighing in on those funds?** **Start with Dr. Wu and Ashley Reed for funds.** **Also ask legislative liaison** **Also ask Dr. Wu about rare disease tne** **Rizwan Hamid, RDAC Member** **Terry Jo Bichell, RDAC Vice Chair** **Kim Stephens, RDAC Member**	
Review of Action Items and Agenda Items for December Meeting	**Scott Strome, RDAC Chair**	