Important notice this is just a draft.

	Draft aHUS Patients' Research Agenda		
	aHUS Registry	**aHUS Global Poll**	**Rare Disease Day Video**
1. Disease onset	• How transient is aHUS due to pregnancy and is there a role for prophylactic eculizumab in some cases?		
	• Does the incidence of aHUS vary in different environments e.g., urban, rural, coastal?		
	• Are hormone changes during key life-stages a significant cause of aHUS onset?		
	• Can boys with aHUS who on-set at a young age grow out of it?		
	• Do annual cycles in immune activity predict		

	a time of year when aHUS onset is more likely?		
	• Are those over 60 years-old with a genetic predisposition but no previous symptoms unlikely to develop aHUS or are they still at risk?		
		• What possible events trigger aHUS? • Is there a comprehensive list of triggers of aHUS? • Why do triggers cause aHUS in some but not others? • Are multiple triggers at the same more likely to result in aHUS?	• Since the complement system is suppressed in infants receiving eculizumab , can your child get an active vaccine?
2. Diagnosis	• What are the barriers to diagnosis, and how can they be overcome?	• What is the best way to diagnose aHUS among all TMA's	• How long will it be before all the doctors know about the disease aHUS so they can save more lives?

			• My daughter was originally diagnosed with colitis and days after was diagnosed with aHUS. She had ADAMS13 abnormalities, and elevated complement Bb, SC5b-9, C5a, and C3a levels, she also had mildly decreased ADAMTS13 levels. She was put on Soliris and a week later she passed away after having colon surgery complications. Should she have been diagnosed and put on Soliris sooner? • How many doctors around the world are treating aHUS patients?
	• Can the degree of kidney function recovery be predicted by the time between aHUS onset and diagnosis/treatment?		
	• Is there a “golden period” for diagnosis which can predict more favourable outcomes for patients with aHUS?		

3. Eculizumab treatment	• Is it possible to ensure the effectiveness of eculizumab in the body?	• What is the mortality of aHUS patients despite receiving eculizumab?	
	• For how many days does eculizumab remain effective following administration and does it vary between patients?	• Is stopping treatment an option for specific patients? • Can a list of criteria be established for when eculizumab can be with withdrawn? • Can eculizumab be delivered by a patch for continuous delivery? • Can eculizumab be injected weekly? • Can the interval for infusions be increased?	• I currently receive Soliris infusions every three weeks. I heard that there are trials being done with sub q injections and eight week infusions. When will I know the results? • Has anybody ever suddenly become immune to eculizumab? • I have MS and aHUS so will I ever be able to safely go off eculizumab as I had total kidney failure and with it I was able to go off dialysis? • Can you have an (aHUS) attack while using eculizumab?
		• Can alternatives to Eculizumab be found? • Can Ritixumab be used? • Can a properdine inhibitor effectively treat aHUS on alternative pathway?	• Is there anything being done for the patients like myself who developed an extreme allergy to the medication eculizumab? • My daughter has a Factor H mutation, in the future does it look promising

		• Can a treatment be found which is affordable in all countries such as India? • What are the side effects of treatment? • Can an effective synthetic version of CFH be developed?	that gene therapy/gene editing will be an option for her? • What it will take for everyone to have access to eculizumab? • Will I ever be able to get my medicine eculizumab like a vaccine, a shot to the arm? • Will eculizumab ever be more affordable or available in a shot/injection? I don't like getting the IV every 3 weeks and it's so expensive just to survive. • I was previously told that medicine for aHUS will always be in IV and or injection form. Is this true or is there a possibility that as my son ages he might eventually be able to take a pill? • When will there be a cure? • Will there ever be a painless way to receive Soliris? • When will new treatment be available? • Can Soliris and the combination of blood pressure medicines lead to

			allergies and sensitivities to surroundings? • Can gene therapy be developed to treat aHUS? • Can we expect any medicine for aHUS other than eculizumab? • When drugs in clinical trials become a reality, will they be affordable and will this also drive the cost of eculizumab down? • Will one of these new drugs in the pipeline be more affordable than eculizumab and will the competition bring down the price of eculizumab? • Will eculizumab ever be available in a form other than infusion? • As eculizumab continues to evolve in its method of delivery, will the side effects be similar to eculizumab? Or might there be less side effects? • Where infertility is detected and IVF is indicated, is this a safe course of treatment and how does this interact with eculizumab? • How can our Government think it's fair to put an obstacle between a patient and accessing life saving treatment? I'm lucky enough to have access now, but in January

			2018, it could be different so that stress is always lingering. • I discontinued eculizumab but what is the difference between patients who can and who cannot discontinue eculizumab? • Does your doctor recommend an antibiotic for protection from meningitis (in addition to the vaccine) because it is a side effect of eculizumab? • What are the long term effects of eculizumab infusions? • In the future will Soliris affect in any way? • How long until we know if there are long term side effects to using Soliris? • How likely is it that a child grows an immunity to eculizumab? • Has anybody ever suddenly become immune to eculizumab? • How long will we have to wait for some other form of medicine, instead of an infusion every 2 weeks?

			● As for the drugs in clinical trials, when these become reality, will they be affordable and will this also drive the cost of eculizumab down? ● . How can governments and laboratories be aware of this disease so that everyone can access treatment without question? That no one on this earth can suffer kidney loss and even death ● Does anybody have any side effects from eculizumab e.g. could a lot of stomach pain be due to infusions? ● What do other people do to help when they feel so sick in the few days post treatment? ● Is it possible that there will soon be no discrimination and all patients will have access to their treatment for aHUS, independent of the country they live in? ● Is there any way out for patients who can come out from the dark world of

			ahus in india where we can get access to a low cost drug? • Do doctors recommend an antibiotic for protection from meningitis (in addition to the vaccine) because it is a side effect of eculizumabs? • How and when can we decide to stop Complement Blocking Therapy in aHUS? • What is the risk of relapse under treatment with eculizumab and especially when did it occur after severe episodes in the past? • What happens to us if the ACA (Affordable Care Act) is repealed?
4. Clinical effects	• What are the outcomes of a transplant without eculizumab and what non-kidney damage is likely from any resulting aHUS onset?	• How long prior to a transplant should eculizumab be administered? • Does eculizumab have to be used for a transplant?	

	• What is the incidence of (multi-organ) co-morbidities with aHUS for adults and children?	• Are headaches/migraine, weight gain, confusion and memory issues, hypertension, stomach pains, fungal infections, physical disability and/or anxiety treatments needed after an episode of aHUS? • What is the long term effect of having and being treated for aHUS • Is there a link between aHUS and other auto-immune disorders? • Before aHUS onset migraines and stomach upsets were common but why is that not so after onset and receiving eculizumab? • Does aHUS affect non renal organs at a low level?	• We would like to know what the lasting effects may be on her the older she gets? • How can I understand in simple words, what is happening in my body during this disease? • In the subset of aHUS patients who present with pancreatitis, have any genetic factors or other causes been found for the pancreatic involvement?

	• Are there differences between adults and children in terms of co-morbidities?		
5. Psychological/social effects	• Is there any evidence as to whether not knowing the genetic cause or undergoing genetic testing causes the most anxiety?	• What is best way to counsel patients about their genetics?	
	• What is the impact on the working life of adult patients with aHUS and carers of patients with aHUS?	• Is living with aHUS like living with a disability?	
	• What is the impact on education for children with aHUS?		• When will local infusions centres accept aHUS paediatric patients on eculizumab? • Where do we start or what do we do to make sure he has the proper medical care he needs when he starts at school? • What affect, if any, does aHUS have on physical activity as kids get older?

			. Do you run into difficulties with your children's teachers' not understanding aHUS because it is not always visible? For us, his illness is not seen as serious by his teacher
	• What is the attitude of parents towards genetic screening of children?		
	• What are the comparative self-esteem levels of patients with aHUS undergoing different treatment modalities?		• I can be anything I want to be, not even aHUS can stop me but what are the long term effects of taking eculizumab? • Does having aHUS affect my swag factor? • Do you think we can forget the sadness and focus on fighting against aHUS without fear, forgetting the negative? • When will the Australian government going to stop continuing eculizumab prescriptions in 3 - 6 month doses and playing jeopardy with people's lives? Living knowing you may only have this much time on treatment because they want to "see what happens" if you are discontinued is

			just cruel. This is people's lives, not roulette. • I've had ahus for 2 years now without eculizumab and THANKFULLY without a relapse. Is there any PILL form of Soliris being worked on so my mommy will feel better about letting me start it? (That way she can stop worrying everyday about what might trigger a relapse)
	• To help family planning decision, can a risk matrix of the potential harm to a mother or child be developed?	• Is it safe to become pregnant whilst diagnosed with aHUS? • Is it safe to receive eculizumab while pregnant	• I contracted my disease 6 and a half years ago during the delivery process of my beautiful daughter, will I ever be able to have another child? • Can any moms who had an aHUS attack because of pregnancy delivery ever have kids after? • Is eculizumab safe to take during pregnancy? • Having not found a mutation our daughter we are interested in knowing if she can have children when older and as science progresses. Will we ever know if it will be safe for her and others suffering aHUS to become parents?

			• How safe is pregnancy whilst on eculizumab, to foetus and mother (maternal outcomes) and does being on eculizumab during pregnancy prevent a relapse? Where infertility is detected and IVF is indicated, is this a safe course of treatment and how does this interact with eculizumab?
6. Self-monitoring	• Can a blood test be developed to allow patients in remission to monitor themselves?	• Are there symptoms that are predictive of a more catastrophic aHUS event? • Can aHUS be measured at low levels before kidney damage occurs?	• When is the right time to call up the hospital if I am worried about how I'm feeling? I am so anxious that every feeling of sickness is a sign that this thing is at work inside of me causing damage?
7. Patient differences	• What is the spectrum of the aHUS cohort in each country, and are there significant differences between them?	• How many aHUS patients are there in China? • What is the prevalence of aHUS in Pakistan?	• . How many people in the United States have aHUS and how many live in Nebraska, my home state?
	• Is it possible to predict which patients will have the longest time in	• If someone has aHUS and then gets better, what is the chance of it returning?	• What research is there on relapses in aHUS children who are healthy today?

	remission and which will be at the highest risk on new aHUS onset?	• How likely is aHUS to a reoccur if no genetic defect found?	
	• Does the spectrum of the aHUS cohort in each country change over time?		
	• What is the frequency of my specific genetic predisposition in my country and other countries?		
8 Genetic causes		• Can more genetic reasons for aHUS be found? • Are there genetic mutations in the coagulation system causing aHUS? Can families and siblings be tested for genetic causes? • What causes anti factor h antibodies to be created? • When is aHUS likely to occur if you have a specific genetic mutation?	• With CD46/MCP mutation and not on eculizumab what are the chances of aHUS being triggered again? • Are there long term studies to follow aHUS patient health after acute episodes subside, and for those people who have never had aHUS activity despite their aHUS genetic variant profiles? • If I have (anti) factor H antibodies will all my family members have the same mutation, or can it ever differ? • Some members of my family have been affected by aHUS, whilst others

		• When is aHUS likely to occur if you have a combination of genetic mutations? • Should family histories be studied for how aHUS is passed on? • Why does one sibling with CHFR deletion and CF related antibodies one yet another with the same condition not? • Why is the complement system so vulnerable to genetic changes? • What are epigenetic factors of aHUS? • Does blood type have an effect?	have not; sometimes skipping several generations before reappearing again. Why does that happen in aHUS families? • Is there any knowledge about whether the aHUS gene can skip a generation? • My daughter is part of the 30% with no known mutation. Will we ever know her mutation so her doctors can know what her best treatment is? • I discontinued eculizumab. What is the difference between patients who can and who cannot discontinue eculizumab? • Have they been able to identify more factors that would cause one person to develop aHUS but not a second person, if they both have the same genetic defect, for example factor H mutation?
9 Research Cooperation			• When it comes to Rare Diseases can we have better international collaboration, more access to knowledge and research?