SCGE Phase II Planning Workshop Agenda: Background

The goal of the NIH Common Fund Somatic Cell Genome Editing (SCGE) program is to improve the efficacy and specificity of gene editing approaches to help reduce the burden of common and rare diseases caused by genetic changes. During its first 5-year phase, the SCGE program has been focused on improving delivery systems for the delivery of editors into somatic cells, improving genome editors, developing new methods to assess unintended biological effects, developing better animal models for testing genome editing tools and delivery systems, and disseminating program tools and learnings widely. This first phase of the SCGE program is ending in 2023 and there is a possibility of a second 5-year phase if the scientific and medical opportunities are deemed sufficiently compelling and still appropriate for Common Fund support.

This virtual planning workshop will bring together leaders in the field of genome editing and related fields to discuss challenges and opportunities that could be addressed in a potential second phase of the SCGE program. The discussion will cover a selection of topics related to new technologies and approaches that are necessary to fully realize the promise of genome editing for human clinical application.

Please note that this is a closed meeting and may be attended by invitation only. Please contact mgregory.richards@roseliassociates.com with questions about registration, agenda or other logistics.

SCGE Phase II Planning Workshop Agenda: At-A-Glance

The workshop will take place on April 20th, 2021.

Start time (All times in ET)	Session name	Co-Moderators
10:00	Welcome	Dr. Joni Rutter Dr. PJ Brooks
10:30	**Clinical Trial and Regulatory Innovation**	Dr. PJ Brooks Dr. Katherine High
11:40	Break	
11:50	**Prospects for Advancing *In Utero* SCGE**	Dr. Oleg Mirochnitchenko Dr. Katherine High
1:00pm	Lunch	
1:30	**Gaps and Opportunities in Basic Development and Discovery**	Dr. Betty Poon Dr. Vic Myer
2:30	Break	
2:40	**IND-Enabling Preclinical Tools**	Dr. PJ Brooks Dr. Fyodor Urnov

Start time (All times in ET)	Session name	Co-Moderators
3:40	Break	
3:50	**Issues in Immunogenicity**	Dr. Marrah Lachowicz-Scroggins Dr. Paula Cannon
4:50	Closing	

SCGE Phase II Planning Workshop Agenda: Full Detail

Start time (All times in ET)	Session name	Expected Discussion Topics
10:00	Welcome	• Welcome remarks from the SCGE Program Chair • Introduction to the SCGE Program from the SCGE Program Coordinator • Discussants each introduce themselves (30 seconds each)
10:30 (Morning Slot A)	**Clinical Trial and Regulatory Innovation**	• Can we design gene editing clinical trials that truly leverage the platform capacity of genome editing (especially Crispr-Cas) for multiple diseases at a time? • What kind of existing delivery, editing and preclinical technologies could be utilized in such a trial? • What could be done within the next 5-10 years to conduct, support, enable or de-risk such trials? • How do the known the regulatory concerns regarding genome editing impact clinical trial design? • Open Comments: Other important innovations, opportunities, gaps, or hurdles in SCGE clinical trial design or execution.
11:40	Break	

Start time (All times in ET)	Session name	Expected Discussion Topics
11:50 (Morning Slot B)	**Prospects for Advancing *In Utero* SCGE**	- What is the current status of the *in utero* genome editing field? - What are potential disease conditions/gene targets to be considered for in utero genome editing? How much will selection of the diseases be affected by the well-developed prenatal/genetic diagnosis? - What considerations should be taken in the decision process concerning pediatric, early onset, or late onset conditions? - What are known or potential advantages/ disadvantages of in utero genome editing? - What studies should be conducted to provide additional confidence in a favorable outcome of *in utero* genome editing? - What are the current technical advances for delivery and genome editing which can be used for *in utero* applications (nonviral and viral)? What is missing/needs to be developed/tested? - What will be a good model system to assess pre-clinical *in utero* genome editing safety concerns and effectiveness (ex vivo/animal models)? Should any associated technologies (detection/monitoring systems etc.) be developed? - What regulatory/policy issues should be solved before moving *in utero* genome editing to clinical applications / IND path approvals - Open comments on additional considerations regarding use of *in utero* genome editing, such as: - Selection of gene targets - Timing of the intervention - Safety considerations: - Prenatal/postnatal effects - Mother/fetus effects - Developmental influences - Off target effects (large rearrangements, tissue/cell type specific effects) - Germ cells - What are the immediate steps needed to move forward?
1:00pm	Lunch	

Start time (All times in ET)	Session name	Expected Discussion Topics
1:30 (Afternoon Slot A)	**Gaps and Opportunities in Basic Development and Discovery**	• Do you have the enzyme(s) you need to make the edit you want to make? Are they active enough? • Can you deliver the enzymes you work with to the cell types and tissues relevant for the disease(s) you are interested in? Do you have access to relevant primary cells and/or tissues? • Do we need our systems to be transient, inducible or reversible? • Do you have the ability to assess the safety of formulation/vehicle and route of administration? Is the vehicle itself going to be problematic? • Do the current standards for discovery and validation of off targets exist to the satisfaction for clinical advancement? Do we have the tools and knowledge to ask and answer the risk-benefit question to the satisfaction of the patient, physician, and researcher? How (should) we handle the personal genome of the patient? Do we have the tools to do so? • Do we have the appropriate assay systems to measure cellular and animal PK to determine appropriate dose estimation? Do we need better tools to do so?
2:30	BREAK	

2:40
 	
(Afternoon Slot B)
	IND-Enabling Preclinical Tools	• What benchmarks are needed to be achieved to meet preclinical safety requirements and for IND application/approval?
		• How can we streamline the pathway to IND application/approval?
		• How do we address human genetic variation in considering the off-target profiles of gene editors in order to safely enter the clinic?
		• State of assay development:
		  ○ Are additional assays needed for potential clinically relevant toxicities of genome editing?
		  ○ Are additional in vitro assays needed in human cell systems in a manner that meets regulatory needs form the outset, and that will reduce the need for clinically relevant animal toxicity testing? Especially in large animals?
		  ○ Can we develop novel, highly sensitive functional assays that assess the oncogenic potential of gene editor off-target effects, given that such events may be very rare (>1/million cells)?

3:40	Break	

Start time (All times in ET)	Session name	Expected Discussion Topics
3:50 (Afternoon Slot C)	**Issues in Immunogenicity**	• What are the gaps in strategies to overcome potential immune response to genome editing (including responses to the editing enzyme, to the delivery vector and to the therapeutic gene itself)? • Can we develop better strategies for limiting the immune response to gene editing in vivo, so we are only delivering to the intended target cells? (could be through modification of the vector or of the editor) • What "immunological" considerations should we account for to understand the immunogenicity of all components of editing machinery and long-term transgene expression? • What is the impact of delivery modality for editing machinery on short and long-term safety (mode of delivery, delivery carrier, type of vector on inflammation and off-target effects)?
4:50	Closing	• Thanks and Closing Remarks