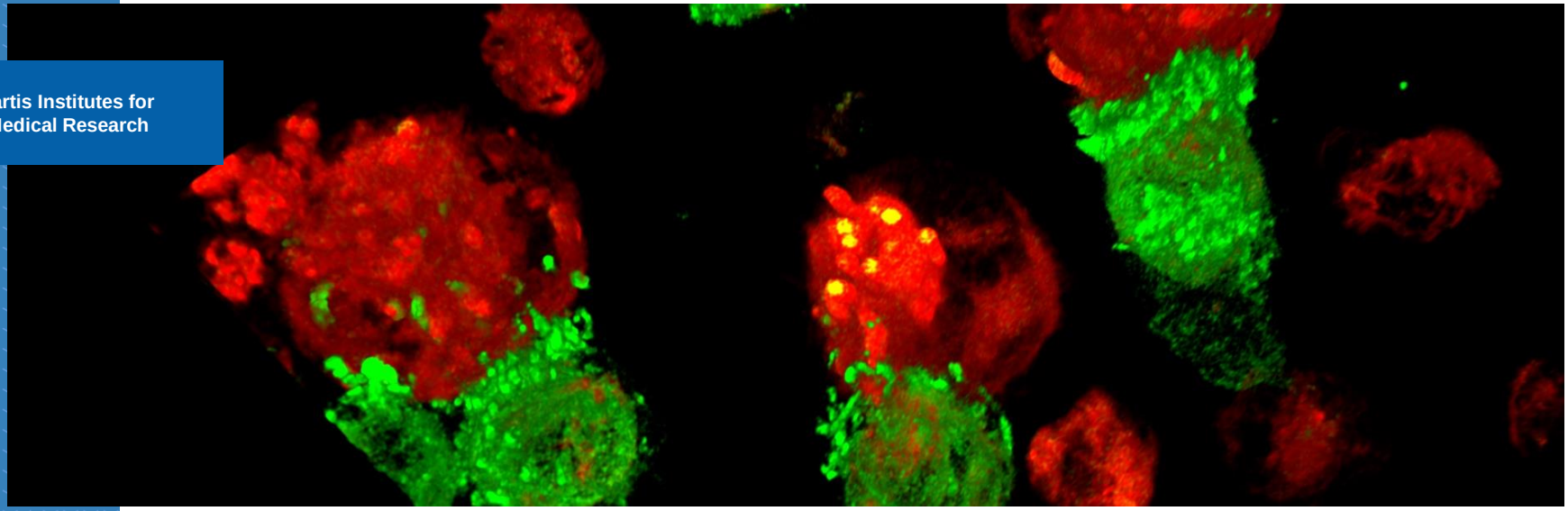
Novartis Institutes for BioMedical Research

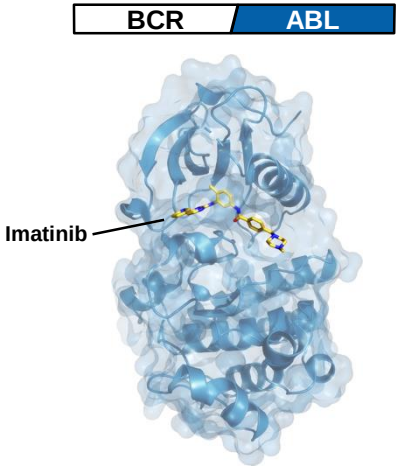


Cell & Gene Therapy Introduction

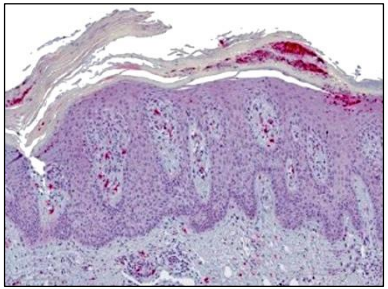
Jay Bradner, M.D.

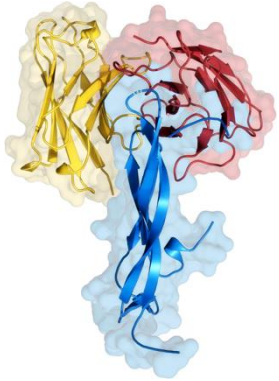
Media Event Annual Results Conference
January 29, 2019

NOVARTIS



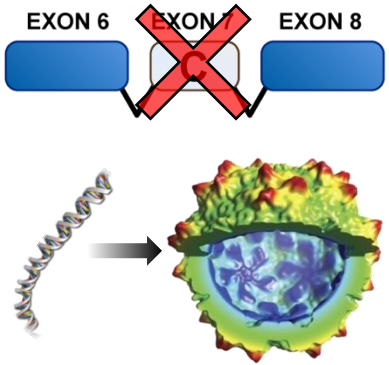
Psoriasis
IL-17 IHC



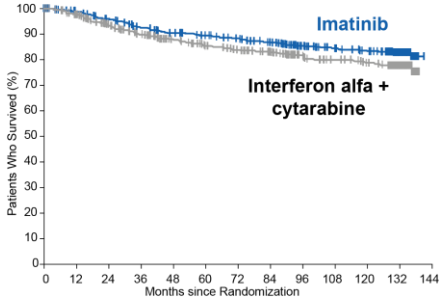


IL-17 + Secukinumab Fab

SMN1 Gene

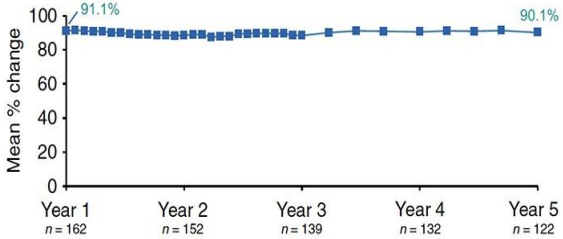


Overall survival @ 10 Years, CML



Hochhaus et.al., NEJM 376;10 March 9, 2017

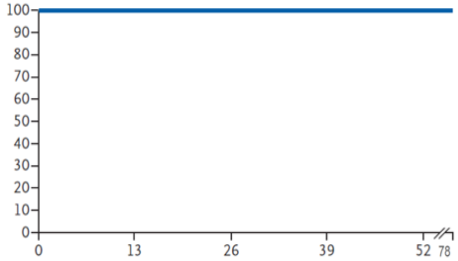
Mean % improvement from baseline, PASI



As-observed analysis with n being the number of evaluable patients; PASI, Psoriasis Area and Severity Index score

Bissonnette et al., JEADV 2018, 32, 1507–1514

Probability of event-free Survival, %

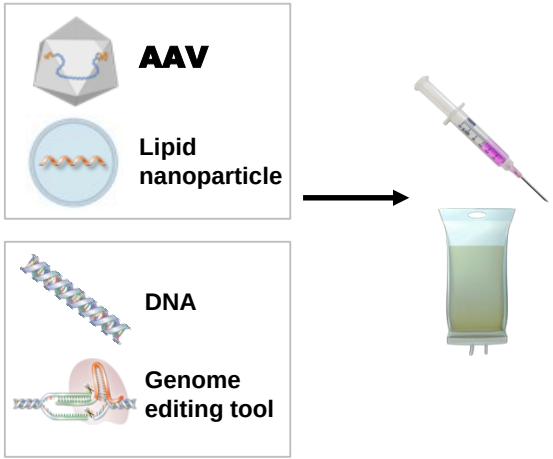


Mendell JR, et al, N Engl J Med 2017; 377:1713-1722

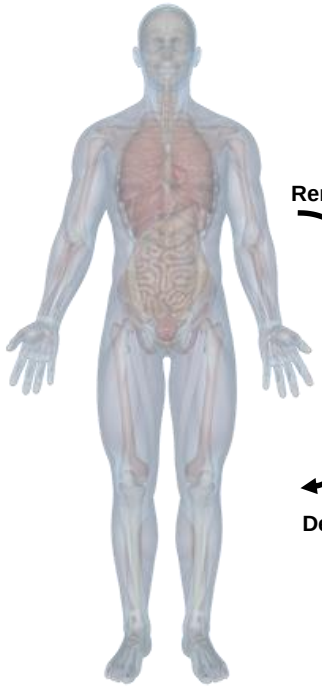
Landscape of Cell & Gene Therapies

In Vivo

Direct gene delivery to patient

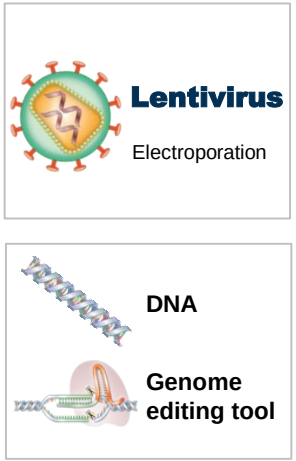


Dominant current delivery vector: AAV



Ex vivo (= Gene-modified cells)

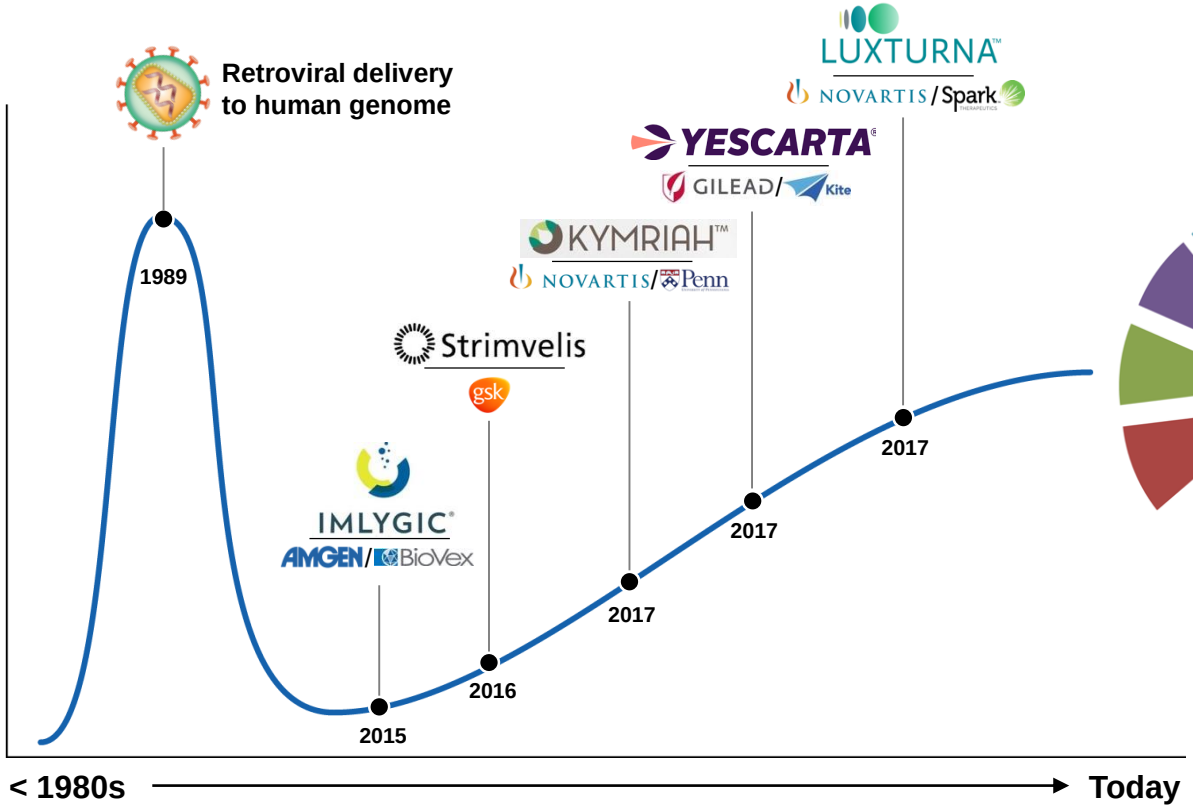
Gene delivery to cells outside the body

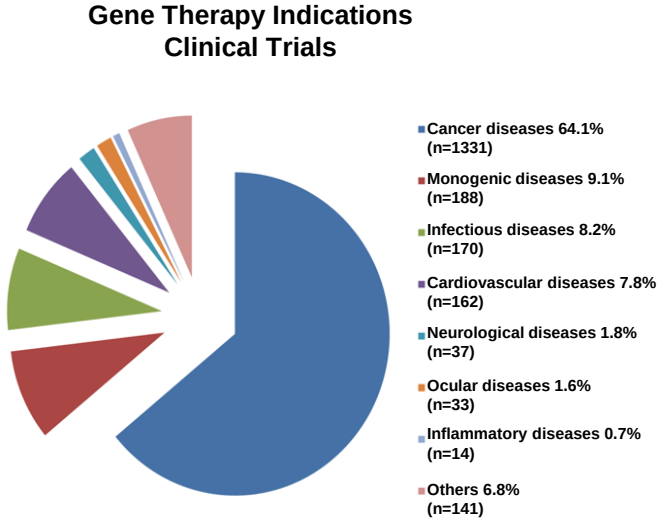


Dominant current delivery vector: Lentivirus

Note: AAV = adeno-associated virus

Cell & Gene Therapies Come of Age





Villate-Beitia et al. 2015. Intech.

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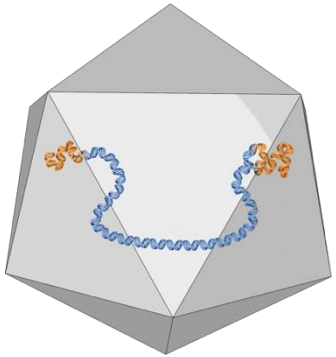
Cell & Gene Therapy @ Novartis

Strategic growth area for development of transformative medicines

AAV



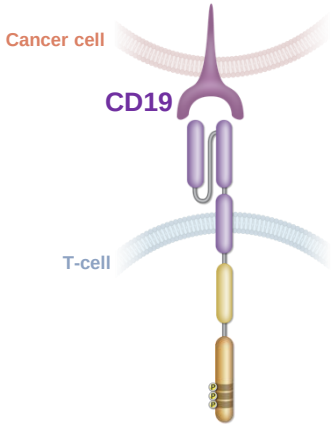
avexis

Spark THERAPEUTICS

Neuroscience

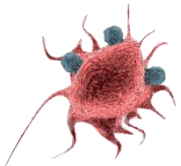
Ophthalmology

CAR-T



Penn University of Pennsylvania

Intellia THERAPEUTICS

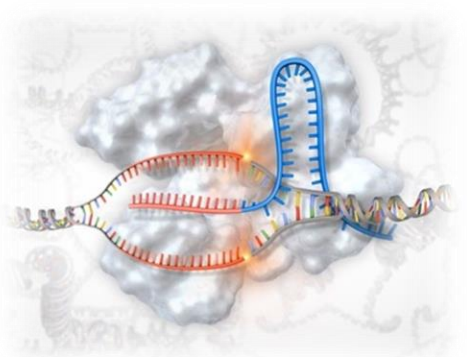


B-Cell malignancies

AML

Solid tumors

CRISPR



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Intellia THERAPEUTICS

Hematology

Ophthalmology

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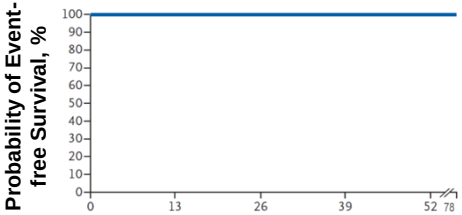
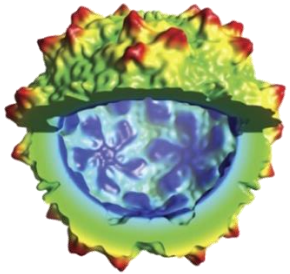
Adeno-Associated Virus (AAV) Gene Therapy

Neuroscience

AVXS-101 - Spinal Muscular Atrophy



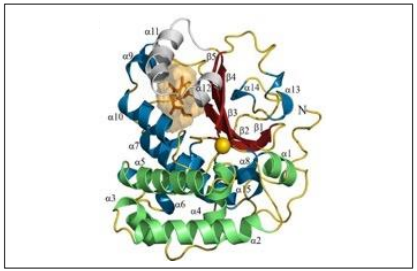
Mendell JR, et al, N Engl J Med 2017; 377:1713-1722

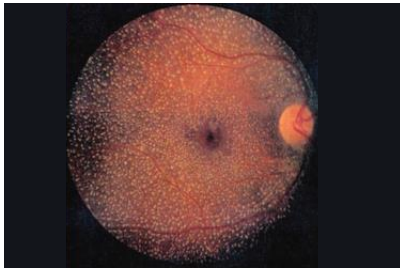


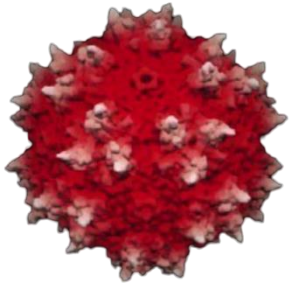
Recombinant AAV9 Capsid Shell

Ophthalmology

CPK850 - Retinitis Pigmentosa

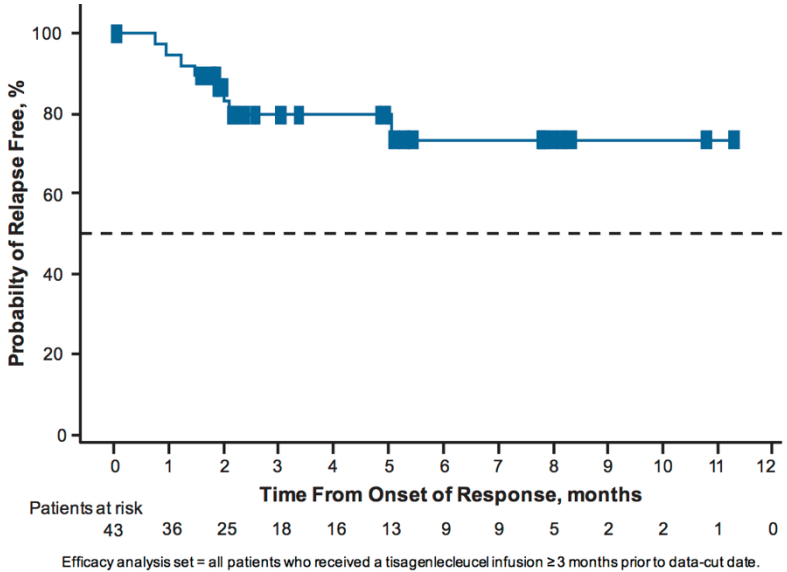




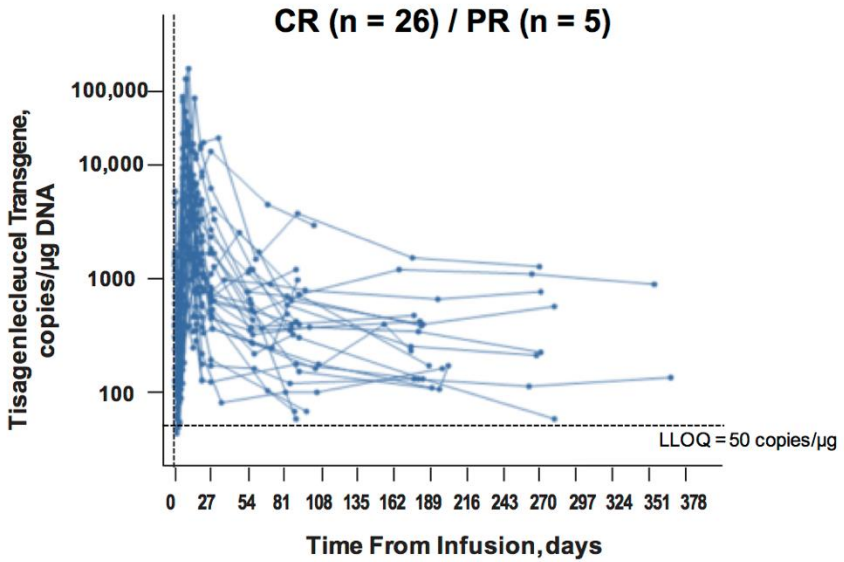


AAV8-RLBP1 vector

CAR-T Therapy



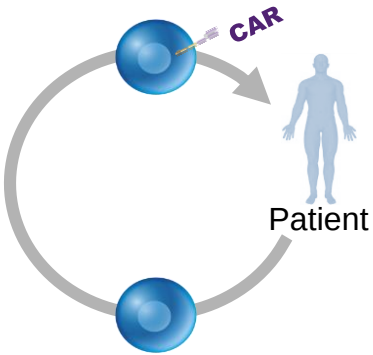
Efficacy analysis set = all patients who received a tisagenlecleucel infusion ≥ 3 months prior to data-cut date.



Stephen Schuster and JULIET Study Investigators, ASH 2017

Next Generation CAR-T Therapy

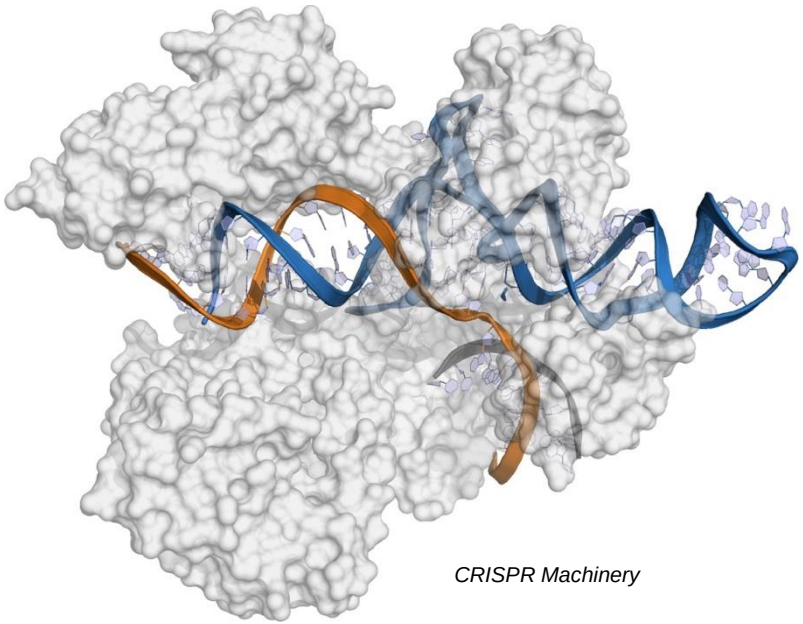
Improving patient accessibility



Novartis has one of the most comprehensive CAR-T R&D programs across multiple indications

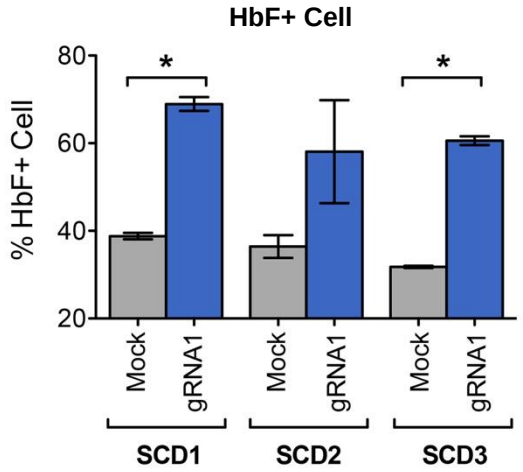
CAR-T type	Indication	Phase 1	Ph 2/Pivotal	Phase 3	Submitted	Approved
CD19 CAR-T	Pediatric & young adult r/r ALL					US, EU
CD19 CAR-T	r/r DLBCL					US, EU
CD19 CAR-T	DLBCL in 1st relapse			Starting 2019		
CD19 CAR-T	r/r FL		Started 2018			
CD19 CAR-T	r/r DLBCL in combination with pembrolizumab	Started 2018				
CD19 CAR-T	Adult r/r ALL			Starting 2019		
CD19 CAR-T	r/r CLL combination with ibrutinib		Starting 2019			
CD19 CAR-T	Pediatric NHL		Starting 2019			
CD19 CAR-T	1st L high risk pediatric and young adult ALL		Starting 2019			
CD19 CAR-T	r/r DLBCL combo with ibrutinib		Starting 2019			
Other targets (UPenn partner)	BCMA&CD19, CD22&CD19, CD123, EGFRv3	Started 2018				

CRISPR/Cas9 Gene-Edited Hematopoietic Stem Cell Therapy for Sickle Cell Disease



CRISPR Machinery

Increase in F-Cell Number and HbF Expression Upon Editing of SCD Patient PB Derived CD34+ Cells



N=3/experiment, 4 independent experiments, data show mean+SEM

CARIBOU BIOSCIENCES

Intellia THERAPEUTICS

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The Future Of Cell & Gene Therapy

The promise

- Potentially transformative
- Clarified target guidance from human genetics
- Potential for one time therapies
- Work across multiple therapeutic areas
- Platforms capable of multiple medicines

The challenge

- New emerging therapies
- Not trivial to manufacture at scale
- Immuno-reactivity
- High cost of goods