Cellastra

Strategic Report 3/11/2020

TOP GENE THERAPY COMPANIES

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- Review of companies using:
  - Gene modified cell therapy / CAR -T Cell
  - Gene vector transfer – incl.. AAV, ceDNA
  - “Gene editing” -incl.. CRISP, mRNA

EXECUTIVR SUMMARY

Executive Summary (1)

1. Gene Modified Cell Therapy CAR-T - COMPANIES
   - Patient's own T cells are modified in the lab: chimeric antigen receptor (CAR) T Cells - Gene that encodes for a specific tumor antigen is incorporated in the T-cells- these are reinfused into the patients where they multiply thousand fold– Bind specifically to the tumor surface and become activated
   - Revolutionary cancer treatment: Complete response rate > 80% in acute lymphoblastic leukemia (ALL) and overall response rate of 50% in myeloma – solid tumors pending
   - 08/2017 FDA approved Kymriah (Novartis), and **escarta (Kite acquired for 30 B by Gilead), JUNO acquired for 9 B by Celgene which on 11/119 closed acquisition by BMS for 75B.**
   - Cost: 376-475K/for one "curative" treatment

2 A) Adeno Associated Virus (AAV) and other gene vector s
   - 12/2017 FDA approved Luxturna (SPARK), AAV2 vector
   - ➢ Hemophilia next in line but many players
   - ➢ Hemophilia A: BioMarin, Generation Bio
   - ➢ Hemophilia B: SPARK, Freeline, UniQure
   - ➢ **05/24 2019 FDA approved AveXis AAV9 based product ZOLGENSMA (onasemnogen abeparvovec; AVXS-101) for pediatric patients with Spinal Muscle Atrophy (SMA)**

Most companies focus on rare or ultra rare genetic diseases (metabolic, CNS etc). Programs seem overlapping and competitive
   - In Feb 2019 : Failjures reported by GeneSight (Lebers disease) and by Sangamo (MPS II) –
   - Ultra rare diseases tricky – UniQure did not renew license for Glyberra (first gene therapy approved in EU (2012) (only 31 pts treated and 30 of them in clinical study) – price of 1.5M USD led to bankrupt ion of Amsterdam Molecular Therapeutics (AMT) in 2015
   - BioMarin (Market cap **15B,** Sales 1.3B and 2,500 employees globally) still world leader in rare diseases with 7 drugs on the market but none of them so far gene therapy.

Large Indications so far:
   - Parkinson: Voyager, Axovant, Prevail
   - Heart Insufficiency: UniQure

MOST COMPANIES TARGET RAR MONMOGENEIITALRRECT A CONGENEITAL GENE DEFECT

   - **CELLASTRA UTILIZES GENE VECTOR TECHNOLOGY TO PROGRAM E.G. SKIN CELLS IN THE WOUND FTER BURNS AND SUSRGERY TO ENABLE ROBUST ENDOGENOUS EXPRESSION/ SYNTHESIS A POTENT ANTI -SCARRING PEPTIDE AT SITE OF TH WOUND FOR EFFECTIVE SCAR PREVENTION THROUGHOUT THE HEALING PROCESS**
   - **HUGE INDICATIONS WITH GREAT UNMDET NEED**

2 B) Other Gen eVectors – ceDNA ("Close ended DNA) –Generation Bio:

"can move from the cytoplasm of the cell into the nucleus without a virus. It has been dubbed GeneWave technology, and the company believes it avoids the immune response that can be toxic in AAV-based gene therapy approaches

Executive Summary (2)

3. Gene Editing companies

A) CRISP : "Clustered Regulatory Interspaced Short Palindromic Repeats "

[Palindromic =symmetric sequence which reads identical from one end or the other e.g. MADAM]

- Small DNA fragments found within prokaryotes (primitive cells e.g. bacterial – remnants from a previous virus infection of e.g. a bacterium
- Used as a marker to detect and destroy DNA from similar viruses during subsequent infections
- Thus, plays a key role in the anti-viral defense of prokaryotes such as bacteria.
- CRISPR/Cas9 I (=CRISP Associated Nuclease 9) is a revolutionary technology that allows for precise, directed changes to genomic DNA.
- CRISP/Cas9, when paired with a guide RNA, cuts double-stranded DNA allowing for specific changes to DNA. These site-specific DNA modifications can be utilized to carry out sophisticated gene knock-outs or knock-ins.

- Patents filed in parallel by two group and no interference claim upheld and confirmed by US Appeals Court 10/2018:

- Patent filed by UC Berkeley/U of Vienna licensed to Caribou, CRISPR, Casebia, Intellia = companies involved in CAR-T, hemoglobinopathies, and rare diseases etc

- Patent filed by Broad Institute (MIT) licensed to Editas (and used in JUNO Car T cell program)

B) ZINC FINGER NUCELASE (ZFN) TECHNOLOGY: Older, predates CRISP and considered to be more time consuming, expensive and difficult and less selective for targeted edits.

- Sangamo – founded 1995

C) Stem Cell editing: Also older technology - placing a healthy gene into the patient's extracted bone marrow stem cells, and transplanting these corrected stem cells back into the patient

- Bluebird – founded 1992 -Universal Cell 2013

Executive Summary (3)

3. [Gene Editing companies continued{

D) <u>mRNA TECHNOLOGY : Also predates the CRISP revolution</u>

“can direct the body’s cellular machinery to produce nearly any protein of interest, from native proteins to antibodies and other entirely novel protein constructs .”

- MODERNA with market cap of 3.9 B has raised 3.2 B in venture funding and licensing deals with AZ, Merck, (immuno oncology/ vaccines), DARPA grants (infectious diseases) Vertex etc. , /Rare diseases in deal with Alexion and separate venture (Epidera)
- Translate Bio – Rare diseases

<u>Useful Resources</u>

- **New NIH Gene Terapy Institute**
- **New FDA Guidelines on Gene therapy**
- **ARMs State of the Industry Report 2020**
- **Gene therapy Market approvals**
- **Successful Exits**
- **Frecent Licensing Deals**
- **Manufacturing News**

USEFUL RESOURCES

Useful Resources

Resource	Ref
Alliance of Regenerative medicine (ARM) – state of the Industry report 1/13/20	https://46ax7g7nqmq3divu13d9zsn1-wpengine.netdna-ssl.com/wp-content/uploads/2020/01/State-of-the-Industry-FINAL.pdf
FDA Final Guidelines on gene therapy 2/2020	https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances
New NIH Institute for Gene Therapy 2/19/20	https://www.gene-therapies.org/post/new-institute-launched-to-ensure-the-u-s-healthcare-system-is-ready-for-gene-therapies

Gene Therapy Market Approvals (1)

Date	Agency	Agent	Company	Indication	Price/ treatm.	Comment
11/2012	EMA/EC	Glyberra	UniQure	lipoprotein lipase deficiency (LPLD) Ultra rare disease	1M USD	Company discontinued launch
12/2017	FDA	Luxturna	Spark	Leber's hereditary optic neuropathy;	425,000 USD	11/2018 Novartis gets approval in EU
08/2017	FDA	Kymriah (CAR-T)	Novartis	ALL (acute lymphoblastic leukemia)	475,000 USD	80% response rate; only responders have to pay 2018/05 approved in Non Hodgkin Lymphoma (NHL)
10/2017	FDA	Yescarta (CAR-T)	Kite (Gilead)	B Cell Lymphoma	373,000 USD	

Gene Therapy Market Approvals (2)

Date	Agency	Agent	Company	Indication	Price/ treatm.	Comment
08/2018	FDA and EMA	Onsattro (anti sense) (*Alnylam in EU)*	Amylam	Poly-neuropathy ITTR amyloidosis	450.000 USD/ year	RNAi therapeutics Dosed once weekly sub cut.
10/2018	FDA	Tegsedi (anti sense)	Akcea and Ionis	ITTR amyloidosis Poly-neuropathy	450.000 USD/ year	RNAi therapeutics Approved by EMA in 07/2018 Dosed once weekly sub. cut.
5/2019	FDA	Zolgen-sma	AveXis (Novartis)	Spinal Muscle Atrophy (SMA)	1. M USD(5 annual installments of 300,000)	
6/2019	EMA	Zynteglo	Bluebird	Betha thalassemia (transfusion resistant)	TBD	Manufacturing delaying launch to 2020

Successful Exits (1)

Comp.	Founded	Funding	Asset	Exit	Price	Acquirer
Kite	2009	• 4 rounds raised 85.3 M • IPO 06/2014 raised 127 M	CAR T Yescarta appr.09/2017	**10/2017**	30 B	Gilead
Juno	2013	• 3 rounds raised 310 M • IPO 12/2014 raised 264.6 M	CAR-T NHL BLA	01/2018	9 B	Celgene
AveXis	2013	• 5 rounds raised 75.1 M • IPO 02/2016 raised 95 M	AVX-101 SMA - Spinal Muscle atrophy	04/2018	8.7 B	Novartis
Celenex	(Spin off from Children's Hospital/OH	• Gene therapies for lysosomal storage diseases / funding not disclosed	Up to 10 indications	09/2018	100M upfront	Amicus
Spark	2013	• 2 rounds raised 122.8 M • IPO 01/2015 raised 161 M	Luxturna approved 09/2017	Acquisition completed 11/20/2019	4.3 B	Roche

Successful Exits (2)

Comp.	Founded	Funding	Asset	Exit	Price	Acquirer
NightStar	2013	• 5 rounds raised 174.6 M • IPO 09/2017 raised 75 M	Genetic blindness	03/2019	800 M	Biogen
Exonics	2017	• 45M (incl. Ser. A in 11/2017)	CRISP /musc.dystr	06/2019	245M	Vertex
Audentes	2013	• Ser. A, B, C 137.5 M • IPO 2016 75M	AAV9 muscle dis.	12/2019	3-B	Astellas
Qiagen	1986 in EU. HQ in Hilde Germany And Venlo, The Netherlands	• 1006 IPO NYSE • Several funding rounds • 26 acquisitions	Testing kit corona virus; mol. diagnistics	03/03/2020	11.5 B	ThermoFisher

Recent Licensing Deals

Company	Details	Date	Price	Acquirer
Voyager	Strategic license to Neurocrine for clinical development in Friedrich ataxia and parkinson	2019/01	$165 million in cash including a $115 million upfront payment and a $50 million equity investment.	Neurocrine
Oxford Biomedica	Exclusive worldwide license using lenti viral vector in Parkinson	2019/03	$842.5 M total; $30 M upfront	Axovant

Gene therapy Manufacturing News

- 5/2019 ThermoFisher has acquired Brammer Bio in up to 1.7B deal to access plants in Cambridge, MA and Florida with 380 employees
- 5/2019 Catalent has acquired Paragon Bioservices in 1.2B deal to access plant in Baltimore with 380 employees
- 8/2019 Pfizer to invest 500M in Sanford Facility, NC
- 11/2019 Fujifilm to invest 119M USD (13B Yen) into GMP facilities for gene and cell therapieies at Fujifilme Diosynth Biotechnology (FDB) College Station, Texas and Hillerod, Denmark
- 01/30/2020 Hitachi announces new facility in Allendale, NJ for manufacturing cell & Gene therapies and hire up to 500 employees
- 02/2020 Audentes announces plan to invest $109M to build new manufacturing plant in Sanford,NC

REVIEW OF COMPANIES

Gene Modified Cell Therapy

CAR –T COMPANIES

Novartis Gene Therapy

Founded	Unit founded 2012
Based	
Ownership	
Business Model	For Profit
Valuation	
Financials	
Lead Product	Kymriah
Product Type	CAR-T
Stage	approved
Indications	B-cell ALL ; NHL (DLBCL)
website	Novartis.com

Key Events

- 2012 deal with U of Pennsylvania to acquire global rights to CAR-T technology developed by Carl June. – financials not disclosed
- CAR = chimeric Antigen Receptor
- From patients white blood cells Genetically modify T-cells to recognize tumor antigen CD-19
- "Turns the T-cells into hunter / attack cells that attacks the cancer cells"Each CAR-T cell can multiply to an army of 10,000 attack cells.
- 83 % complete response rate in children with ALL (acute lymphoblastic leukemia)
- **2016: Gene therapy unit integrated with the company**
- **2017/08 Kymriah Approved by FDA based on a study in 82 pts, supported by historical data in about 90 patients with more than 90 % Complete response rate.**
- **2018/05 second indication : NHL (DLBCL) approved by FDA based on overall response rate of 50 percent (incl.. 32% complete responses) in 68 refractory/relapsed pts in international MC trial\Price tag of 475,000 USD /patients / no charge if the patient does not respond. [value based pricing strategy]**
- Sales 2019 projected to reach 200 M USD New indications to follow; Multiple Myeloma other hematol malignancies and solid tumors. 2019 Novartis makes offer to acquire

Kkey people

- **Carl June, Inventor, U of Pennsylvania**
- **Mike Perry, DVM, Sr VP, CSO until 2017**
- **Pascal Touchon, SVP,Global Head Cell& Gene Therapy until 2019**

Kite Pharma (Gilead/BMS)

		Key Events	Kkey people
	2009	• founded in 2009 by Arie Belldegrun, M.D., FACS, an Israeli-American oncologist, who served as the company's chairman, president and chief executive office • CAR-T Technology • Kite Pharma, founded in 2009, is a clinical stage biopharmaceutical company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patients own immune system to eradicate cancer cells • they are developing a pipeline of product candidates for the treatment of advanced solid and hematological malignancies using their therapeutic platform – engineered Autologous Cell Therapy (eACT™) – in which a patient's own T cells, or white blood cells, are engineered to recognize and destroy their cancer. • 7 programs in helmatol. malignancies Ph. 1, 2 and one in Ph. 3 • 10/2017, Kite Pharma's therapy, Yescarta (axicabatagene ciloleucel) became the first CAR-T therapy approved by the FDA for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. • 10/2017 acquired by Gilead for $30B • **12/11/2019: BLA submission to FDA for approval of KTE-X19 in mantle Cell Lympoma (MCL)**	• Arie Belldegrun, M.D., FACS, an Israeli-American oncologist, who served as the company's chairman, president and chief executive officer, Founder:
Based	Santa Monica, CA		
Ownership	Acquired by Gilead in October 2017 for $30 B		
Business Model	For Profit		
Valuation	At IPO 6/2014 $625 M		
Financials	3/2011 Ser.. A $15 M 12/2012 Debt Fin. $250 K 5/2013 Ser.. A $20 M Alta Partners 4/2014 Venture Round $50 M IPO 6/2014 raised $127 M Delisted 8/2017		
Lead Product	Yescarta approved 10/2017 LBCL		
Product Type			
Stage			
website	https://www.kitepharma.co		

JUNO Therapeutics

	2013
Based	Seattle, WA
Ownership	Acquired by Celgene in January 2018 for $9 B
Business Model	For Profit
Valuation	At IPO 12/2014 $1.7 B
Financials	12/2013 Ser.. A $120 M 4/2014 Ser.. A $56 M Bezos Expeditions, Venrock 8/2014 Ser.. B $134 M IPO 12/2014 raised $264.6 M Delisted 3/2018
Lead Product	
Product Type	CAR-T
Stage	
Indications	NHL
website	Celgene.com

Key Events

- founded in 2013 through a collaboration of the Fred Hutchinson Cancer Research Center, Memorial Sloan-Kettering Cancer Center and pediatrics partner Seattle Children's Research Institute. The company was launched with an initial investment of $120 million, with a remit to develop a pipeline of cancer immunotherapy drugs. The company raised $300 million through private funding and a further $265 million through their IPO.
- In December 2014 the company signed an agreement with Opus Bio, Inc for a chimeric antigen receptor (CAR-T) cell product candidate targeting CD22.
- In April 2015 the company entered into a collaboration with MedImmune (a subsidiary of Astra Zeneca) investigating combination treatments for cancer. The trials will assess combinations of MEDI4736 and one of Juno's CD19 directed chimeric antigen receptor T cell candidates. In May 2015, the company announced its intention to acquire Stage Cell Therapeutics for up to $223 million.[5] Later in the same month the company launched a collaboration, with Editas Medicine, to create CAR-T and high-affinity T cell receptor therapies to treat cancer. In June, 2015 the company announced a 10-year partnership with Celgene valued at $1 billion.
- On January 22, 2018 Juno Therapeutics was acquired by Celgene for 9B USD.
- **January 2019 announced Celgene to be acquired by BMS in 74B USD stock deal.**

Kkey people

- **Funders: Isabelle Rivière, Michael Jensen, Michel Sadelain, Phil Greenberg, Renier Brentjens, Stan Riddell**

Autolus Therapeutics

		Key Events	Kkey people
	2014	• Autolus is applying its broad array of T cell programming technologies and capabilities to engineer precisely targeted controlled and highly active T cell therapies that are designed to better recognize cancer cells, break down their defense mechanisms and attack and kill these cells • Founded on advanced cell programming technology pioneered by Dr Martin Pule and was spun-out from University College London in 2014. • Since its inception, the company has undergone rapid growth, systematically adding the capabilities needed to manufacture and develop its programmed T cell product candidates. • "they have developed their own proprietary viral vector and semi-automated cell manufacturing processes, which they are already using in their clinical-stage programs" • No clinical l pipeline announced	• Dr Christian Itin • Chief Executive Officer and Chairman of the Board of Directors • Previously he was Chief Executive Officer and Chairman of the Board of Directors of Cytos Biotechnology Ltd, a public biotechnology company that merged with Kuros Biosurgery Holding Ltd, and he now serves as Chairman of the Board of Directors of the merged entity, renamed Kuros Biosciences Ltd. • President and Chief Executive Officer of Micromet Inc., a formerly Nasdaq-listed biopharmaceutical company which was acquired in March 2012 by Amgen, Inc. for USD 1.2 billion in cash. Micromet pioneered T-cell engaging antibodies with blinatumomab first approved product in this field. • Co-founded Zyomyx, Inc., a protein chip company based in Hayward, CA, USA. • PhD in cell biology from U Basel
Based	London, UK		
Ownership	**NASDAQ AUTL**		
Business Model	For Profit		
Valuation	IPO 6/2018 $657 M Market Cap 10/2019 $50 M		
Financials	1/2015 Ser.. A £30 M 3/2016 Ser.. B £40 M Arix Bioscience, Woodford Investment Management 9/2017 Ser.. C $80 M Cormorant Asset Management IPO 6/2018 raised $150 M		
Lead Product	Follow on: 2/2020 74M		
Product Type	CAR-T		
Stage			
Web site	www.autolus.com		

Atara Biotherapeutics

		Key Events	Kkey people
Founded	2012	• A leading off-the-shelf, allogeneic T-cell immunotherapy company developing novel treatments for patients with cancer, autoimmune and viral diseases. • Our off-the-shelf, allogeneic T cells are bioengineered from donors with healthy immune function and allow for rapid delivery to patients. • Originating from over a decade of groundbreaking clinical experience at Memorial Sloan Kettering and QIMR Berghofer, Atara's T-cell immunotherapies are designed to precisely recognize and target cancerous or diseased cells • Atara's off-the-shelf, allogeneic T-cell immunotherapy in development, tabelecleucel, or tab-cel® (formerly known as ATA129), is being developed for the treatment of patients with Epstein-Barr virus (EBV) associated post-transplant lymphoproliferative disorder (EBV+ PTLD), as well as other EBV associated hematologic and solid tumors, including nasopharyngeal carcinoma (NPC). • Also developing off-the-shelf, allogeneic ATA188 and autologous ATA190 T-cell immunotherapies using a complementary targeted antigen recognition technology for specific EBV antigens believed to be important for the potential treatment of multiple sclerosis (MS). • License agreement with Memorial Sloan Kettering Cancer Center; license, and research and development collaboration agreement with QIMR Berghofer Medical Research Institute; and strategic collaboration with H. Lee Moffitt Cancer Center.	• Founding CEO:: Dr. Isaac Ciechanover, MD, MBA. Previously, he was a partner in the life sciences practice at Kleiner Perkins Caufield & Byers. Earlier as Celgene's Executive Director for Business Development, he spearheaded the company's venture capital efforts and led licensing and M&A activities with an aggregate value of more than $6.7 billion. Isaac has also held business development and venture capital roles at Amylin Pharmaceuticals, Pequot Ventures' healthcare practice and Pfizer. an M.Phil. in Epidemiology from Cambridge University, an M.D. from Weill Cornell Medical College and an M.B.A. from Harvard Business School. • Pascal Touchon, new CE0 fr. June 2019; prev. head of Novartis Cell& Gene Therapy Unit and 30 year in pharma incl. Glaxo Wellcome • Dietmar Berger was Head R&D 5/2018-5/2019; prev. Genentech, Bayer, Amgen, prof hemonc in Freiburg
Based	San Francisco		
Ownership	**Nasdaq; ATRA**		
Business Model	For Profit		
Valuation	**Market Cap 10/2019 $585 M**		
Financials	Total cash raised: $59 M (incl.. 52M in IPO in 2014)		
Lead Product			
Product Type	T-cell; CAR-T		
Stage			
Indications	See table		
website	Atara.com		

Cellectis

		Key Events	Kkey people
Founded	1999	• Cellectis has 20 years of expertise in gene editing based on its flagship TALEN® technology and pioneering electroporation system PulseAgile. This enables us to develop a new generation of immunotherapy product candidates with additional safety and efficacy attributes and equip them to resist mechanisms that inhibit immune system activity. • Cellectis is the pioneering gene editing company, deploying core proprietary technologies to develop off-the-shelf immunotherapies to target and eradicate cancer cells TALEN® • This ultra-precise gene-editing technology makes it possible to precisely edit the genome of any organism. • UCART (Universal Chimeric Antigen Receptor T-cells) are “off-the-shelf” allogeneic products, whose production can be industrialized and thereby standardized with consistent pharmaceutical release criteria, over time and from batch to batch. Paradigm shift in terms of ease of use, availability and the drug pricing challenge. - all allogeneic CAR T-cells engineered to be used for treating the largest number of patients with a particular cancer type. Each UCART product candidate targets a selected tumor antigen and bears specific engineered attributes, such as compatibility with specific medical regimens that cancer patients may undergo. UCART is our first therapeutic product line that we are developing with our gene editing platform to address unmet medical needs in oncology. • he UCART123 clinical trial in AML, AMELI-01, is a Phase 1, dose escalation study n January 2020 at MD Anderson Cancer Center. • 202/02 deal with Servier Euro 25M uipfront plus 370M in milestone paymnets for CAR-T targetin CD-19	• Chairman of the Board of Directors and CEO is **André Choulika** • **Philippe Duchateau, CSO** • **Bill Monteith** • **Executive Vice President, Technical Operations**
Based	Paris, France		
Ownership	**NASDAQ Global :CLSS** **Market cap 611M 03/06/2020**		
Business Model			
Valuation	**For Profit**		
Financials			
Lead Product			
Product Type	CAR-T		
Stage			
Indications	AML		
website			

AdVerum

		Key Events	Kkey people
Founded	2006	• Founders: Mark S. Blumenkranz, Mitchell Finer, Steven D. Schwartz, Thomas W. Chalberg • Formerly Avalanch Biotechnologies. A clinical-stage gene therapy company targeting unmet medical need in ophthalmology and rare diseases. It develops gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. T • Leveraging its next-generation adeno-associated virus (AAV)-based directed evolution platform to engineer AAV capsids with enhanced tropism for certain tissues and improved antibody neutralization profiles over existing AAV variants. • ADVM-022 in wet AMD Phase 1	**Leone Patterson. CEO** • **joined2016 as CFO and CEO since May 2018,** • **. Previously, CFO Diadexus, Inc. Transcept Pharmaceuticals, Inc. ,Exelixis, Inc. and Novartis AG as vice president of global business planning and analysis after working at Chiron, which was acquired by Novartis. Executive M.B.A. from St. Mary's College. Ms. Patterson is also a Certified Public Accountant (inactive status).** **Aaron Osborne, MBBS CMO 2019.** • **Prev (NHS as an ophthalmologist. Dr. Osborne brings previous experience from Genentech, Phase II and Phase III studies in wet age-related macular degeneration (AMD) and diabetic macular edema (DME),** • **Previously, Alcon. And Novartis ophthalmic programs at Novartis, where he led the medical oversight of Lucentis' late-stage development an**
Based	Menlo Park, CA		
Ownership	**NASDAQ ADVM Market cap 767M 03/06/2020**		
Business Model	For Profit		
Valuation			
Financials	RAISED 70M over three prevrounds. Raised 150M piublic offering closed 202/0214		
Lead Product	ADVM-022		
Product Type	AAV based engineering		
Stage			
Indications	Wet AMD		
Web stie	Adverum.com		

GENE VECTOR COMPANIES

Spark Therapeutics (ROCHE)

		Key Events	Key People
Founded	2013	• Founded in March 2013 by **Katherine High, MD (Director Ctr for Cell.&Mol. Therapeutics, Children's Hospital Philadelphia CHOP)Jeffrey Marrazzo, and Steven Altschuler, MD, (President & CEO CHOP**) as a result of the technology and know-how accumulated over two decades at Children's Hospital of Philadelphia (CHOP),	Jeff Marrazzo , Co-founder, CEO • MBA Wharton, MPH arvard, • Led the creation and growth of Spark Therapeutics from a research center within the Children's Hospital of Philadelphia to a fully integrated, commercial gene therapy company , secured more than $1 billion in capital and built an organization of more than 325 colleagues. Katherine High, MD, Cofounder, President &CSO 2013-02/2020 **Kathy Reap, MD CMO** until 3/2020, Prev Sr VP A;;ergan and Actavis **John Takefman, Head of Regulatory** 214-03/2020, prev 15 years with FDA
Based	Philadelphia, PA	• At Spark Therapeutics, a fully integrated company committed to discovering, developing and delivering gene therapies, they challenge the inevitability of genetic diseases, including blindness, hemophilia and neurodegenerative diseases.	
Ownership	**Acquisition by Roche announced in February 2019 and completed November 2019 – 4.3B USD**	• they have successfully applied their technology in the first FDA-approved gene therapy in the U.S. for a genetic disease, and currently have three programs in clinical trials, including product candidates that have shown promising early results in patients	
Business Model	For Profit For Profit	• 2017/12 FDA approved LUXTURNA (voretigene neparvovec-rzyl) intraocular suspension for subretinal injection	
Valuation	At IPO 1/2015 $352 M Market Cap 10/2019 $4.2 B	• 2018/01 Novartis licensed Lucturna for territories outside US 2018/11 Novartis gets approval by European Commission (EC)	
Financials	10/2013 Ser.. A $50 M Children's Hospital of Philadelphia 5/2014 Ser.. B $72.8 M Sofinnova Investments IPO 1/2015 raised $161 M	• One treatment – cost $425,000 USD	
Lead Product	Luxturna	• Fidanacogene elaparvovec, previously known by its study ID number SPK-9001,[6] is an experimental drug under investigation for treatment of hemophilia B	
Product Type	AAV2		
	Leber's hereditary optic neuropathy; hemophilia B		
website	www.sparktx.com		

AveXis (**Novartis**)

lan		Key events	Keypppeople
Founded	2013	AveXis was founded by John D. Harkey, Jr., their former Chairman, in 2013. Under Mr. Harkey's leadership, they formed a collaboration with National Children's Hospital (NCH), Philadelphia, to explore the use of gene therapy for the treatment of Spinal Muscle Atrophy (SMA) and secured their first institutional investors and expanded their leadership team. their current operations are a result of this collaboration with NCH and research conducted by their Chief Scientific Officer, Dr. Brian Kaspar. Dr. Kaspar has over 20 years of gene therapy experience,	• John Lennon, PhD, President since 6/2018; Novartis 11 years incl. Head Oncology Japan/US, VP New Products and Portfolio Strategy; McKinsey 4 years • Brian Kaspar, CSO, and Alan Kaspar, Head of Research, left the company in May 2019, after investigation of preclinical data breach. • investors including funds and accounts managed by Adage Capital Management, L.P., Boxer Capital of Tavistock Life Sciences, Deerfield Management, Foresite Capital Management, LLC, Janus Capital Management LLC, QVT Financial LP, RA Capital Management, Roche Finance Ltd, Rock Springs Capital Management • April 09, 2018 (GLOBE NEWSWIRE) -- Novartis will acquire AveXis for $218 per share or a total of $8.7 billion in cash. Completed in May 2018 • 02/2019 Novartis invests 200M USD in building a manufacturing plant employing more than 200 people.
Based	Bannockburn, IL		
Ownership	Acquired by Novartis in April 2018 for $8.7 B		
Business Model	For Profit		
Valuation	At IPO 2/2016 $430 M		
website	www.avexis.com/	• In 2014 license of NAV AAV9 gene vector from REGENXBIO for treatment of spinal muscular atrophy (SMA) Type 1. • The company also intends to expand the study of gene therapy into other types of SMA and two additional rare neurological monogenic disorders: Rett syndrome (RTT) and a genetic form of amyotrophic lateral sclerosis (ALS) caused by mutations in the superoxide dismutase 1 (SOD1) gene. The U.S. Food and Drug Administration (FDA) has granted AVXS-101 Orphan Drug Designation for the treatment of all types of SMA and Breakthrough Therapy Designation, as well as Fast Track Designation, for the treatment of SMA Type 1. The European Medicines Agency (EMA) also granted AveXis access into its PRIority MEdicines (PRIME) program for AVXS-101 for the treatment of SMA Type 1. • **On 5/24/19 FDA approved the product ZOLGENSMA for pediatric patients with SMA , Q4 sales $186M**	

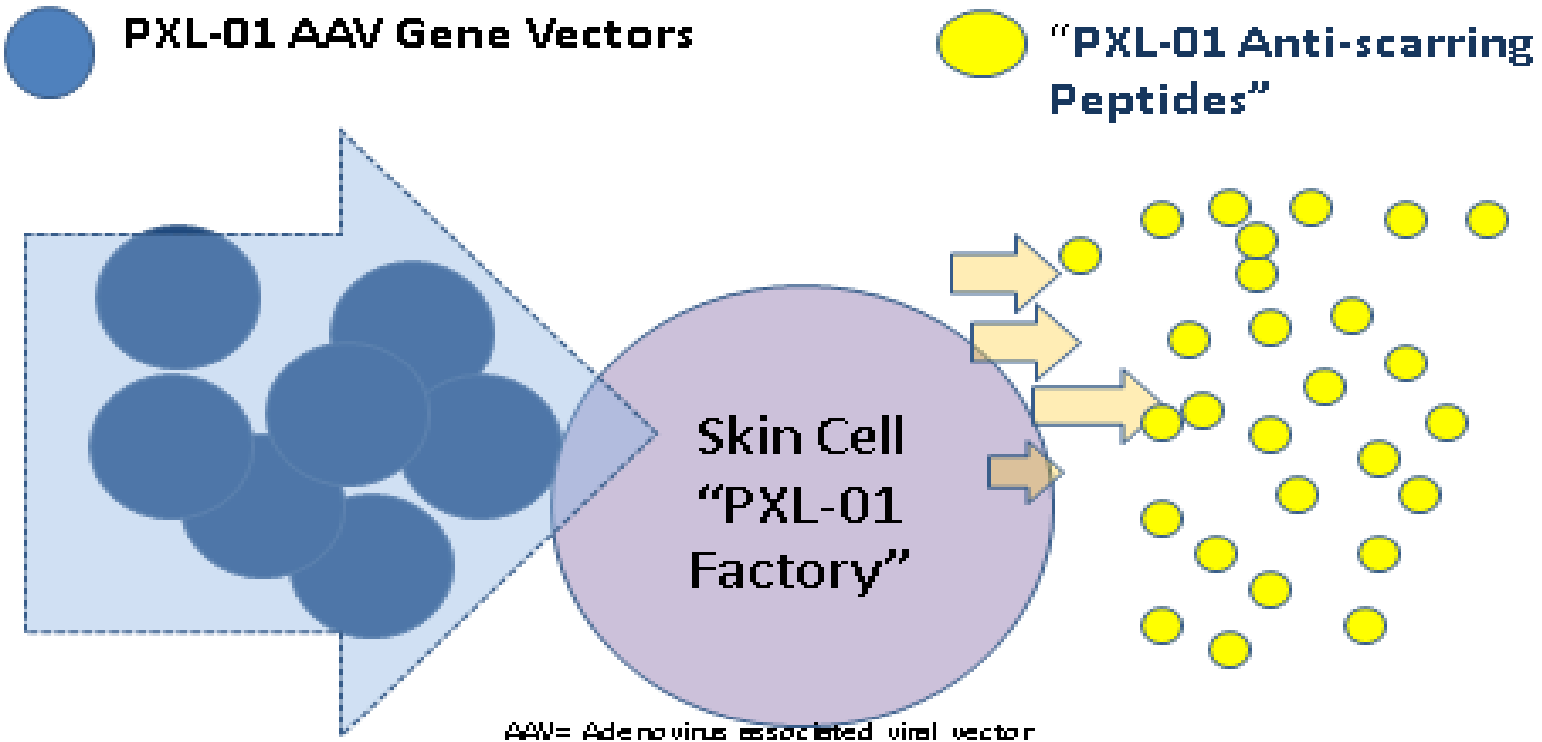
FerGene (Ferring Spin Out)

		Key Events	Key People
Founded	2019	• **FerGene is an new Gene therapy, spin off Ferring Pharmaceuticals. has been created to potentially commercialize nadofaragne firadenovec in the US and to advance the global clinical development.** • **A replication-deficient recombinant adenovirus encoding human interferon alpha-2b with potential antineoplastic activity. Upon intravesical administration, nadofaragene firadenovec infects nearby tumor cells and expresses INF alpha-2b intracellularly which activates the transcription and translation of genes whose products mediate antiviral, antiproliferative, antitumor, and immune-modulating effects** • **Nadofaragene firadenovec – a 150 patient Phase 3 study completed in patients with BCG unresppnsive bladde rcancer**	• **On Dec 19, 20019 nnounced the appointment of David Meek as President and Chief Executive Officer, effective January 14, 2020.** • **Mr. Meek has 30 years of industry y, he has served as CEO of Ipsen, a leading global biopharmaceutical company focused on innovation and specialty care and dedicated to improving lives through the discovery of new medicines in oncology, neuroscience and rare diseases.**
Based	Saint-prex, Vaud, Switzerland		
Ownership	**Ferring invested 400 M USD** **Black Stone Life Sci 170M USD**		
Business Model	For Profit		
Valuation			
Financials			
Lead Product	Nadofaragene firadenovec		
Product Type	Recombinant AAV virus		
website	FerGene.com		

Cellastra Inc.

		Key Events	Key people
Founded	**2005**	• Recent announcements • 03/03/3030: Ce;;astra announces lomng term from in-vivo transgene expression of proprietary anti-scarring peptide • **12/15/2019: Cellastra announces results from in-vivo transgene expression of proprietary anti-scarring peptide. Preparing for clinical study in burn injuries** • 07/15/2019 : Cellastra announces filing of global patent application for prevention of scars and adhesions • .06/24/2019: Cellastra announces collaboration with leading academic laboratory in Canada for manufacturing and testing of a novel gene vector programmed for scar prevention. Preparing for clinical study in burn injuries. • s04/04/2019: Cellastra announces updates from American Burn Association's Annual Meeting in Las Vegas, April 2-5, 2019. Prof. Folke Sjoberg , Cellastra Scientific Advisory Board Memberawarded to give the Everett Idris Evans Memorial lecture on frontiers in burn injury treatment. • 01/07/2019: Cellastra announces 10M USD Series A capital call to support new gene therapy program for scar prevention after surgery and burn injuries. Appoints gene therapy leadership in new management positions. • 12/01/2018: Cellastra announces the appointment accounting veteran Bruce Phillips as new Chief Financial Officer	• **Karl Mettinger MD, PhD, Cofounder , President & CEO since 2011, 35 biotech veteran: (Kabi/Pharmacia (acquired by Pfizer), IVAX (acquired by TEVA), Supergen/Astex (acquired by Otsuka), PAssociate Prof\Karolinska Institute** • **Brad Thompson, PhD, CTO , board member, inventor of CELLEXA platform. Cofounder President& CEO Kickshaw Ventures, 35 year biotech veteran incl. Chair of BIOTECanada.** • **Henrik (Hanks) Kulmala, PhD, Sr VP Product Development & RA 35 year biotech veteran incl. Fujisawa/** • **Alan Llewis, PhD, Exec. Chairman, 40 years Bniogech incl. VP R&D at Wyeth, President Research Div., Celgene, CEO Signal (acquired by Celgene), NovoCell, Ambit (acquired by Daichii), MediStem (acquired by Intrexon),** • **Sven Andereasson, BIOD, 40 year biotech veteran, in l Kabi/Pharmacia (acquired by Pfizer, CEO Iscanova (acquired by NovaVax where he is currently Sr VP Corp Development** • **Daniel Quintero, General Counsel, Secretary, Founding Partner and MDPrometheus Partners,**
Based	**San Francisco**		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials			
Lead Product	CELLEXA		
Product Type	Recombinant AAV6.sFF gene vector programmed for local anti scarring peptide production in a wound area		
Stage			
Indications	Scar / adhesion prevention after burn injuries/ surgery		
website	www.cellastra.com		

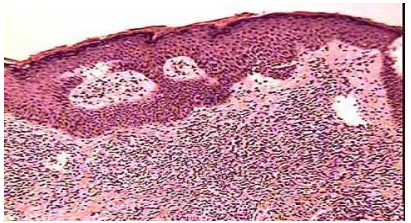
CELLEXA


PXL-01 AAV Gene Vectors
"PXL-01 Anti-scarring Peptides"
Skin Cell "PXL-01 Factory"
AAV= Adenovirus associated viral vector
PXL01= Lactoferrin sub peptide sequence

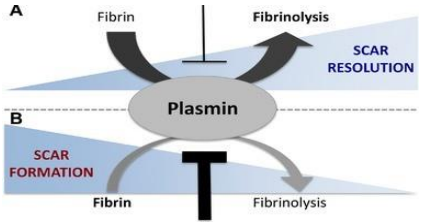
PXL-01 Anti-scarring Mechanisms

PXL-01

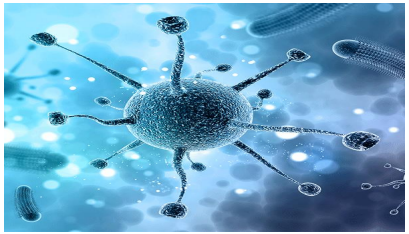
Attenuates Inflammation



Attenuates fibrin formation



Anti-microbial

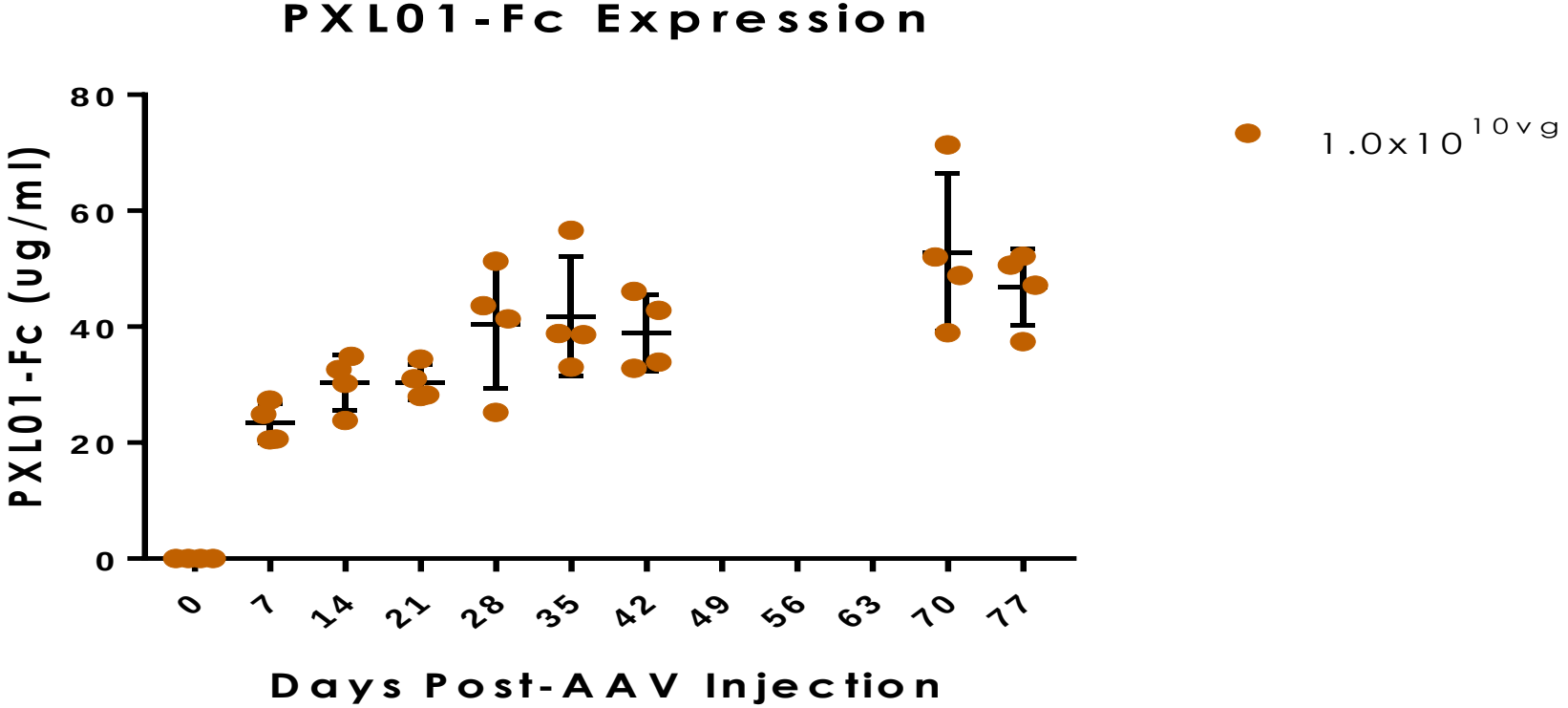


Nilsson E et al, Ann Surg . 2009,250(6):1021-8.

Robust Expression of PXL01 ≥77 Days

PXL01-Fc Serum Concentrations (i.m. Admin)

Fc tag added to enable quantification of expression



REGENXBIO

		Key events	Keypppeople
Founded	2009	▪ Novel AAV (NAV) Technology Platform (licensed from U of Penn, developed in James Wilson's Lab)n consists of exclusive rights to AAV7, AAV8, AAV9, AAVrh10 and over 100 other novel AAV vectors (NAV Vectors). We currently have exclusive rights to over 100 patents and patent applications worldwide covering our NAV Vectors, including composition of matter claims for AAV7, AAV8, AAV9 and AAVrh10, as well as methods for their manufacture and therapeutic uses. We believe this patent portfolio forms a strong foundation for our current programs and with our ongoing research and development, we expect to continue to expand this robust patent portfolio. ▪ The foundation of our NAV Technology Platform was discovered in an effort to identify next generation AAV vectors that could overcome the limitations of earlier generation AAV vectors (AAV1 through AAV6). • **Sex programs in Phase1/2 and a number of preclinical programs**	• Founders: Scientific founder James Wilson, U Penn. • Cofounders: James Brown, Kenneth Mills Ken Mills: President and CEO, prev. with diagnostic companies MesoScale Diagnostics and Igen International. S.B. in chemistry from the Massachusetts Institute of Technology.
Based	Rockville, DC		
Ownership	**NASDAQ RGNX**		
Business Model	For Profit		
Valuation	Market Cap 10/2019 $1.5 B		
Financials	5 rounds raise $118.9 M IPO 2018/08 raised $201.8 M		
Lead Product			
Product Type	AAV Vectors 7, 8 ,9, 10		
Stage			
Indications			
website	Regenxbio.com		

REGENXBIO PIPELINE

- RGX 314 wet age-related macular degeneration (AMD). Ph. 1/2a
- RGX121 MPS II Phase 1-2
- RGX 111 MPS I Phase 1-2
- RGX 181 Late-infantile neuronal ceroid lipofuscinosis Type 2 (or CLN2 disease) Preclin.
- RGH 501 HoFH Ph. 1-2

2017/08/25 Acquired Dimension Therapeutics for 85M USD, with two AAV gene therapy products at IND stage (DTX 301 and DTX401 , both with Orphan rug status for metabolic diseases –ornithin transcarbamylas e(OTC) deficiency, and glycogen storage disease, respectively.

UniQure N.V.

		Key Events	Key People
Founded	2012	• UniQure is a leader in the field of gene therapy and developed the first and currently the only gene therapy product to receive regulatory approval in the European Union. • they are developing a pipeline of adeno-associated virus (AAV)-based gene therapies both internally and through multiple collaborations. they develop their gene therapies using their innovative, modular technology platform, including their proprietary manufacturing process. • they initially focus on orphan diseases, but through their multiple collaborations and the recent acquisition of the cardiology gene therapy company InoCard they have made the next step towards developing gene therapies targeting chronic and degenerative diseases that affect larger populations • Bristol-Myers Squibb and UniQure announced in April 2015 an agreement that provides BMS exclusive access to UniQure's gene therapy technology platform for multiple targets in cardiovascular diseases (for Congestive Heart Failure) as well as the potential for target-exclusive collaboration in other disease areas. • Proof-of-concept in hemophilia B, and preclinical proof-of-concept in Huntington's disease.	• Matt Kapusta • Chief Executive Officer • Mr. Matthew Kapusta joined uniQure as their chief financial officer in January 2015 and was elected to their Management Board at the 2015 annual general meeting. In December 2016 he was appointed their chief executive officer. • Collaboration agreements with 4 D Molecular Therapeutics and SyPromics regarding gene vectors expression
Based	Amsterdam, Netherlands and Lexington, MA		
Ownership	**NASDAQ QURE**		
Business Model	For Profit		
Valuation	At IPO 2/2014 $235 M Market Cap 12/20/2019 $3.0 B		
Financials	7/2013 Private Equity Round $58 M Collar Capital IPO 2/2014 raised $88.5 M		
Lead Product	Glybera –first approved gene therapy – withdrawn from market		
Product Type			
Stage			
Indications			
website	http://uniqure.com/		

Glybera –1st EU Approved Gene Therapy

- **Gene therapy to reverse lipoprotein lipase deficiency (LPLD), a rare inherited disorder which can cause severe pancreatitis.**
- **1986, Michael R. Hayden and John Kastelein began research at UBC, confirming the hypothesis that LPLD was caused by a gene mutation. ULTRA RARE DISEASE PREVALNCE 1-2 PTS PER MILLION POPULATION**
- **2002, Hayden and Colin Ross successfully performed gene therapy on test mice to treat LPLD; their findings were featured on the September 2004 cover of Human Gene Therapy.**
- **Kastelein—who had, by 1998, become an international expert in lipid disorders—co-founded Amsterdam Molecular Therapeutics (AMT), which acquired rights to Hayden's research with the aim of releasing the drug in Europe.**
- **In July 2012, the European Medicines Agency recommended it for approval (the first recommendation for a gene therapy Endorsed by the European Commission in November 2012. Initial price tag 1.6M per treatment (60 i.m. injections).**
- **AMT went bankrupt and in 2015 the assets acquired by UniQure and drug relaunched at 1M USD/treatment**
- **2017 UNIQURE DECIDED NOT TO RENEW THE APPROVAL WITHDRAWN FROM MARKET –ONLY 31 PTS TREATED – ONLY ONE PATIENT HAD BEEN TREATED OUTSIDE A CLINICAL TRIAL**

BioMarin

	1998
Based	Novato, CA
Ownership	**NASDAQ BMRN**
Business Model	Fully Integrated, 2,500 employees globally
Valuation	Market Cap 15.1 B12/20/2019
Financials	IPO 7/1999 raised $58.5 M 2017 $1.3 B in total revenues
Lead Product	7 on the market
Product Type	Gene therapy for hemophilia A
Stage	Phase 3
Indications	
website	www.biomarin.com

Key Events

- **So far only one gene therapy project (Hemophilia A)**
- BioMarin is a world leader in developing and commercializing innovative biopharmaceuticals for rare diseases driven by genetic BioMarin has seven products on the market
  - Naglazyme® (galsulfase) - Mucopolysaccharidosis VI (MPS VI),
  - Aldurazyme® (laronidase) - (MPS I) Firdapse® (amifampridine phosphate) (currently approved in the EU only) - Lambert-Eaton Myasthenic Syndrome (LEMS) in adults, a rare autoimmune disease with the primary symptoms of muscle weakness.
- **Hemopjhilia A Gene therapy:**
- Study 270-301: A Phase 3 Open-Label, Single Arm-Study To Evaluate The Efficacy and Safety of Valoctocogene Roxaparvovec (BMN 270), an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII in Hemophilia A Patients with Residual FVIII Levels ≤1 IU/dL Receiving Prophylactic FVIII Infusions

Kkey people

- **Jean-Jacques Bienaime – CEO since 2006**
- **2002 to April 2005, Genencor, acquired by Danisco enterprise value of over $1.2 billion.**
- **1998 to late 2002, Sangstat acquisition by Genzyme Corporation.**
- **1992 to 1998, several senior management positions at Rhone-Poulenc Rorer Pharmaceuticals (now SanofiAventis), position of Senior Vice President of Worldwide Marketing and Business Development responsible for launch of Lovenox® (and Taxotere® (for breast and lung cancer) worldwide.**
- **Genentech, Inc. in the launch of tissue plasminogen activator (t-PA) for the treatment of heart attacks.**
- **M.B.A. from the Wharton and a degree in economics from the École Supérieure de Commerce de Paris.**

UltraGenyx Pharmaceutical

		Key Events	Key People
Founded	2010	• After stepping down as CSO of BioMarin for 12 years Dr. Kakkis went on to found UltraGenyx in 2010 to focus on developing many rare and ultra-rare disease therapeutics. The company went public in January 2014 (RARE; NASDAQ). S • Grown to more than 500 employees developing treatments for seven clinical stage rare and ultra-rare diseases and has now received approvals for two new products for rare diseases, Crysvita® for XLH and Mepsevii® for MPS VII. The company works on rare metabolic, bone, muscle and neurologic diseases with no approved treatments. • 2017 acquisition of gene therapy Dimension Therapeutics for 150 M USD **APPROVED:** • Crysvita®(burosumab) X-Linked Hypophosphatemia (XLH); Mepsevii™(vestronidase alfa) Mucopolysaccharidosis 7 (MPS 7) PPELINE Crysvita for Tumor-Induced Osteomalacia (TIO) Ph. 2 • UX007 Long-Chain Fatty Acid Oxidation Disorders (FAOD) GENE THERAPIES: • DTX301 Ornithine Transcarbamylase (OTC) Deficiency Ph. 1-2 • DTX401 Glycogen Storage Disease Type Ia (GSDIa) Ph. 1	• **Emil D. Kakkis, M.D., Ph.D.** • **Chief Executive Officer and President,** Dr. Kakkis is currently Chief Executive Officer, President and Founder of Ultragenyx Pharmaceutical where he leads a team developing and commercializing multiple rare and ultra-rare disease treatments. • Over the last 25 years, Dr. Kakkis is best known for his work developing novel treatments for rare diseases and working on policy issues affecting rare disease treatment development. • He began his work as an assistant professor developing an enzyme replacement therapy (Aldurazyme®) for the rare disorder MPS I. • After joining BioMarin in 1998, Dr. Kakkis guided the development and approval of two more treatments for rare diseases, MPS VI and PKU
Based	Novato, CA		
Ownership	**NASDAQ RARE**		
Business Model	For Profit		
Valuation	At IPO 1/2014 $436 M Market Cap 12/20/2019 $2.1B		
Financials	6/2011 Ser.. A $45 M 7/2012 Ser.. A $15.1 M 12/2012 Private Equity Round $75 M IPO 1/2014 raised $121 M		
Lead Product			
Product Type			
Stage	Clinical		
Indications			
website	www.ultragenyx.com		

Amicus Therapeutics

		Key Events	Key People
Founded	2002	• Amicus Therapeutics is a biopharmaceutical company at the forefront of developing therapies for rare and orphan diseases. The Company has a robust pipeline of novel, first-in-class, small molecules called pharmacological chaperones for the treatment of lysosomal storage diseases (LSDs). These chaperones may offer a dual-treatment approach for Fabry, Pompe, Gaucher and other LSDs. • As orally administered monotherapy agents, pharmacological chaperones are designed to bind to, stabilize and increase the activity of a patient's own misfolded enzyme. In combination with enzyme replacement therapy (ERT), pharmacological chaperones may improve the uptake of the infused enzyme and potentially improve ERT outcomes. • 9/2018 acquisition of Celenex for $452M and gene therapy programs for lysosomal storage disorders, based in Columbus, Ohio, which operates as a subsidiary of Amicus .	• John F. Crowley is our Chairman and CEO. J • His involvement with biotechnology stems from the 1998 diagnosis of two of his children with Pompe disease—a severe and often fatal neuromuscular disorder. • In his drive to find a cure for them, he left his position at Bristol-Myers Squibb and became an entrepreneur as the Co-founder, President and CEO of Novazyme Pharmaceuticals, a biotech start-up conducting research on a new experimental treatment for Pompe disease (which he credits as ultimately saving his children's lives). • In 2001, Novazyme was acquired by Genzyme Corporation and John continued to play a lead role in the development of a drug for Pompe disease as Senior Vice President, Genzyme Therapeutics.
Based	Cranbury, NJ		
Ownership	**NASDAQ (FOLD) IPO 2007**		
Business Model	For Profit		
Valuation	Market cap 12/20/2019 $2..5 B		
Financials	Raised 315N prior to IPO in 2007		
Lead Product			
Product Type			
Stage			
Indications	Lysosomal storage disorders		
website			

Universal Cells, Inc

		Key Events	Key people
	2013	• development stage company based in Seattle, Washington. Their technology is based on intellectual property developed at the University of Washington, and includes methods for genome editing in human stem cells via homologous recombination with recombinant adeno-associated virus (rAAV) vectors. • recombinant adeno-associated virus (rAAV)-mediated gene editing to efficiently edit chromosomal genes without the use of genotoxic nucleases. rAAV vectors are effective and safe, and have been used in numerous clinical trials. • Recombinant Adeno-Associated Virus • Licensed a stem cell-tropic rAAV vector serotype for engineering human pluripotent stem cells. Their technology allows us to produce customized stem cells that contain deletions, insertions, or point mutations at any genomic position. • Unlike nuclease-based genome editing, their approach is not genotoxic. It does not require a double strand break, generate off-target alterations to the genome, or produce unwanted mutations at the target site. It also does not introduce nuclease genes into the cell that may have unintended effects. • their genome editing platform has been used to generate cell lines that do not express human leukocyte antigen (HLA) molecules on their cell surface, which are critical for determining whether donor tissue will be rejected. Human pluripotent stem cells and cells differentiated from those cells fail to elicit an immune response when HLA antigens are missing from their surface.	• Claudia Mitchell is the former CEO and co-founder of Universal Cells Inc. She previously co-founded Halo-Bio RNAi Therapeutics • Ph.D. in Molecular Biology from the University of Paris and an Executive MBA from the Ecole des Ponts Business School, Paris, France. • David Russell is the CSO and co-founder, discovered the rAAV-mediated gene editing technology licensed by Universal Cells, and has used this approach to engineer HLA genes in human stem cells. • 2015 Collaboration agreement w AdaptImmune on allogeneic T Cell development. • 10/2017 agreement with Catapult. Universal Cells to utilize CGT Catapult's induced Pluripotent Stem Cells to create universally accepted cells • 02/2018 acquired by Astellas to produce pluripotent stem cells with reduced potential for immunological rejection
Based	Seattle, WA		
Ownership	**Acquired by Astellas in February 2018 for $102 M upfront + mile stone payments** **Private**		
Business Model			
Valuation			
Financials			
Lead Product			
Product Type			
Stage			
website	http://www.universalcells.com/		

Audentes Therapeutics

		Key events	Key people
	2012 (seeded by Orbited)	• their mission is to bring innovative gene therapy products to patients living with serious, life-threatening rare diseases. 1) WAT342 for the treatment of Crigler-Najjar Syndrome -ultra-rare, severe, debilitating condition that affects skeletal muscles, leading to severe muscle weakness (hypotonia) and profound respiratory distress, often requiring invasive ventilatory support. It affects an estimated one in 50,000 newborn males worldwide, and is caused by mutations in the MTM1 gene. T132 for the treatment of X-Linked Myotubular Myopathy - High levels of bilirubin in the blood and risk of irreversible neurological damage and death. CN is estimated to affect approximately one in 1,000,000 newborns. CN is caused by mutations in the gene encoding the UGT1A1 (resulting in an inability to convert unconjugated bilirubin).AT845 for the treatment of Pompe's disease. a rare, inherited disorder characterized by severe, progressive muscle weakness and respiratory impairment. It is caused by mutations in the gene that encodes an enzyme called acid alpha-glucosidase, also known as GAA - one in every 40,000 births.AT307 for the treatment of CASQ2-related Catecholaminergic Polymorphic Ventricular Tachycardia, an inherited disease caused by mutations in the CASQ2 gene. CASQ2 encodes a protein called calsequestrin 2, which plays a key role in the physiology of calcium release in cardiac muscle cells, and which is required to maintain normal heart rhythm. 2) 2020/02/18: Announces plan to invest 109M to build new	• Matt Patterson is the co-founder of Audentes Therapeutics and has served as Chief Executive Officer since the Company's inception in November 2012. Mr. Patterson is also Chairman of the Board of Directors and formerly served as President until May 2018. He has more than 25 years of experience in the research, development, and commercialization of innovative treatments for rare diseases and has held positions of senior management in both private and public biotechnology companies. Previously Mr. Patterson worked for Genzyme Corporation, BioMarin Pharmaceutical, and Amicus Therapeutics. Prior to Audentes he was an Entrepreneur-In-Residence with Orbited, the world's largest health-care dedicated investment. • The other cofounder was Thomas Schuetz, MD, PhD, also a prev.. Venture Partner with Oorbimed, current CEO of **Compass Therapeeutics.**
Based	101 Montgomery St, San Francisco, CA		
Ownership	**NASDAQ BOLD**		
Business Model	For Profit		
Valuation	Market Cap 10/2019 $1.2B Acquired 12/03/2019 by Astellas for 3B USD		
Financials	7/2013 Ser.. A $30 M OrbiMed 12/2014 Ser.. B $42.5 M Deerfield 10/2015 Ser.. C $65 M Redmile Group, Sofinnova Investments IPO 7/2016 raised $75 M		
Lead Product	See Next column		
Product Type			
Stage	Ph. 1-2 for first two		
Indications			
website	www.audentestx.com/		

Nightstar Therapeutics

		Key events	Keypppeople
Founded	2013	• **Co-founder Matthew J. During, BA fro U Auckland, , fellow MIT in Neuroscience, and Harvard med School in Neology/Neurosurgery. Prof molecular Med U Auckland 1996-2013, visiting professor Oxford University since 2011,also founder of Vector Neurosciences Inc.** • their mission is to maintain and restore sight in patients with inherited retinal diseases. • they are a clinical-stage company focused on developing and commercializing a pipeline of novel and potentially curative, one-time retinal gene therapies for patients suffering from rare inherited retinal diseases that would otherwise progress to blindness, and, for which, there are no currently approved treatments. • their lead retinal gene therapy product candidate, NSR-REP1, is being developed for the treatment of choroideremia (CHM), a rare, degenerative, X-linked genetic retinal disorder primarily affecting males that is caused by a mutation in the CHM gene. • they have an ongoing Phase 3 registration clinical trial, known as the STAR trial, of NSR-REP1 for CHM. they anticipate that STAR study will be fully enrolled by the first half of 2019 and expect the one-year follow-up results of the STAR trial to be available in 2020. they are also currently conducting a prospective, natural history study, known as the NIGHT study, across multiple clinical sites in the United States, Europe and Canada.	• David Fellow, CEO, Board Member since January 2015 and previously served as a non-executive director of Nightstar from February 2014 to January 2015. • Prev. VP of Johnson & Johnson's Vision Care Franchise where he led the global marketing, new product and licensing active • Prior to that he spent over 20 years at Allergan, Inc., where he served primarily in the sales and marketing areas in a number of capacities, including regional president, corporate vice president and senior vice president in locations in North America, Europe and Asia. • B.A. from Butler University and is currently a board member of the Glaucoma Foundation.
Based	London, UK		
Ownership	**Acquired by Biogen in March 2019 for $800 M**		
Business Model	Investors Ser. C incl.. Redmile, NEA, Syncona, Wellington		
Valuation	At IPO 9/2017 $393 M		
Financials	2/2014 Venture Round £12 M 11/2015 Ser.. B $35 M New Enterprise Associates 6/2017 Ser.. C $45 M Redmile Group, Wellington Management IPO 9/2017 raised $75 M		
Website			

Nightstar Pipeline

- Lead product candidate NSR-REP1, -designed to substantially modify or halt the progression of inherited retinal diseases AAV2 vector containing recombinant human complementary DNA, or cDNA, that is designed to produce REP1 inside the eye.

- Choroideremia (CHM) - a rare, degenerative, X-linked genetic retinal disorder primarily affecting males. Ph. 3 based on pos results in Ph. 2/2 published in NEJM, Lancet etc.,

- X-linked Retinitis Pigmentosa (XLRP) - a rare inherited X-linked recessive genetic retinal disorder primarily affecting males.

- Stargardt Disease - The form of Stargardt disease they are targeting is an autosomal recessive disease that is linked to mutations in the ABCA4 gene that are inherited from both parents

Krystal Biotech

		Key events	Keypppeople
Founded	2015	• Our modified HSV-1 is a replication-defective, non-integrating viral vector that can efficiently penetrate a broad range of skin cells. Use of our proprietary, modified HSV-1 as a gene therapy platform has a number of distinct advantages over other viral gene therapy vectors, including: 1) it can be administered topically; 2) it transduces dividing and non-dividing cells, increasing the efficiency of therapeutic gene transfer; 3) it is non-replicating and is diluted by cell divisions, leading to transient transgene expression; 4) its high payload capacity can accommodate large or multiple genes; 5) it allows for repeat administration; and 6) it does not insert itself into, or otherwise disrupt, the human genome. The myriad benefits of our engineered vector make the STAR-D platform a suitable choice for direct and repeat delivery of therapeutic genes to the skin. • KB103 for Dystrophic Epidermolysis Bullosa • KB103 is Krystal's patented lead product candidate that seeks to use gene therapy to treat all forms of dystrophic epidermolysis bullosa, or DEB. KB103 uses Krystal's STAR-D technology to deliver functional human COL7A1 genes directly to the skin of affected patients. The COL7A1 genes then express functional collagen VII to form anchoring fibrils, thus stabilizing the patient's otherwise • 1/24/2020: breaks ground on 2nd commercial manufacct, site	• Chairman & CEO K Krish Krishnan is an accomplished biotech executive. He was specifically involved in two successful IPOs (COO/CFO of New River Pharmaceuticals, Inc., NASDAQ: NRPH) and COO of Intrexon Corporation, Inc., NYSE:XON), approval of the blockbuster drug Vyvanse (for ADHD in 2007) and the sale of New River Pharmaceuticals, Inc. to Shire Pharmaceuticals, plc for $2.6 billion. • Undergraduate degree from the Indian Institute of Technology and a graduate degree in Finance from The Wharton School at U of Penn • Founder and COO : Suma Krishnan has 25 years of drug development experience as Head of Therapeutics at Intrexon Corporation (NYSE:XON). She began her career as a discovery scientist for Janssen Pharmaceuticals, Inc. • Master of Science in Organic Chemistry from Villanova University, an M.B.A. from Institute of Management and Research.
Based	Pittsburgh, PA		
Ownership	**Public Nasdaq KRYS**		
Business Model	For Profit		
Valuation	**991M ; 12/20/2019**		
Financials	IPO 9/2017 raised 45M Sun Pharma Lead investor 114M raised 6/2019		
Lead Product			
Product Type			
Stage			
Indications	Dystrophic Epidermolysis bullosa		
website	Krystalbio.com		

Voyager Therapeutics

		Key Events	Key People
Founded	2013	• ***ONE-TIME DELIVERY. BENEFITS FOR A LIFETIME.***	•**Founders:**
Based	Cambridge, MA	• Strategic collab U Mass Med School (UMMS) and UCSF	•**Krystof Bankiewicz, M.D., Ph.D.** Kinetics Foundation Chair in Translational Research and Professor in Residence of Neurological Surgery and Neurology, University of California at San Francisco
Ownership	**NASDAQ VYGR**	• their pipeline includes VY-AADC01 for Parkinson's disease, which is in an ongoing Phase 1b study with their collaborators at the University of California, San Francisco,	•**Guangping Gao, Ph.D.** Director, University of Massachusetts Medical School (UMMS) Gene Therapy Center & Vector Core; Scientific Director, UMMS-China Program Office; Professor of Molecular Genetics and Microbiology, UMMS
Business Model	For Profit	• preclinical programs VY-SOD01 for a monogenic form of amyotrophic lateral sclerosis (ALS)	•**Mark Kay, M.D., Ph.D.** Dennis Farrey Family Professor, Head, Division of Human Gene Therapy, Departments of Pediatrics and Genetics, Stanford University School of Medicine
Valuation	At IPO 11/2015 $360 M 9Market Cap 12/20/2019 $119 M	• VY-FXN01 for Friedreich's ataxia.	•**Phillip Zamore, Ph.D.** Professor of Biochemistry and Molecular Pharmacology, and Chair of the RNA Therapeutics Institute, University of Massachusetts
Financials	2/2014 Ser. A $45 M Third Rock Ventures 2/2015 Corporate Round $30 M Genzyme 4/2015 Ser. B $60 M IPO 11/2015 raised $70 M	• Voyager innovates and invests in novel adeno-associated virus (AAV) vector engineering and optimization, manufacturing that includes a baculovirus production system for producing AAV vectors at scale in insect-derived cells, and dosing that includes intraparenchymal, intrathecal and intravenous delivery techniques.	
Lead Product		2018 Andre Turenne, MBA, appointed President and Chief Executive Officer, prev.. Genzyme	
Product Type		2019/01 Strategic deal with Neurocrine in Parkinson and Friedrich Ataxia under the terms of the agreement, Neurocrine Biosciences has agreed to pay Voyager $165 million in cash including a $115 million upfront payment and a $50 million equity investment.	
Stage	Ph. 2 in Parkinson	2019/06/19: stagegic pafrtnership with Sanofi Genzyme restructured	
Indications	Prelim. in ataxia		
website	https://www.voyagertherapeutics.com/		

Axovant Gene Therapies

		Key Events	Key People
Founded	2014	• The company was founded by former hedge fund analyst Vivek Ramaswamy[2] in 2014 as a wholly owned subsidiary of Roivant Sciences.[3] • As of 2015 the company's most advanced drug candidate was intepirdine, a potential add-on treatment to donepezil for patients with Alzheimer's disease and patients with dementia with Lewy bodies.[4][2][7] Axovant acquired this molecule from GlaxoSmithKline in December 2014.[8] In July 2017, Axovant announced that the results of a Phase III trial indicated that the drug was not effective for treatment of Alzheimer's disease.[9][10] It also entered clinical trials for dementia with Lewy bodies,[11] which were unsuccessful as well. Consequently, Axovant announced in 2018 that it has discontinued development of this drug.[12] • In 2018, David Hung resigned and Pavan Cheruvu became the new CEO.[19] • In December 2018, Axovant added two gene therapy programs to treat GM1 gangliosidosis and Tay–Sachs and Sandhoff diseases. • AXO-AAV-GM1 delivers a functional copy of the GLB1 gene via an adeno-associated viral (AAV) vector, AAV9, which is effective in crossing the blood-brain barrier and transducing neurons, with the goal of restoring β-gal enzyme activity for the treatment of GM1 gangliosidosis. The gene therapy is delivered intravenously, which has the potential to broadly transduce the central nervous system and treat peripheral manifestations.	• Pawan Cheruwu CEO since 2018 • Health Science Tech MIT and MD from Harvard, 2009 • 2 years management consultant with McKinsey
Based	Bermuda/London/NY		
Ownership	**NASDAQ AXON**		
Business Model			
Valuation	MarFor Profit ket Cap 10/2019 $142 M		
Financials	IPO 6/2015 raised $315 M 01/19/2020 announces pricing of public offering of 14 million shares: $3.75/share		
Lead Product	See pipeline next page		
Product Type			
Stage			
Indications			
website	ttps://www.axovant.com/		

Axovant Sciences

PROGRAM	GENE	INDICATION	RESEARCH	PRE-CLINICAL	CLINICAL	MARKETED
AXO-AAV-GM1	*GLB1*	GM1 gangliosidosis				
AXO-AAV-GM2	*HEXA/HEXB*	Tay-Sachs and Sandhoff diseases (GM2 gangliosidosis)				
AXO-LENTI-PD	*AADC/TH/CH1*	Parkinson's disease				
AXO-AAV-OPMD	*PABPN1*	Oculopharyngeal muscular dystrophy				
AXO-AAV-ALS	*C9orf72*	Amyotrophic lateral sclerosis				
AXO-AAV-FTD	*C9orf72*	Frontotemporal dementia				

Abeona Therapeutics

		Key events	Key people
	1989	• Abeona Therapeutics Inc. is a clinical-stage biopharmaceutical company developing gene therapies for life-threatening rare genetic diseases. Abeona's lead programs include: • ABO-102 (AAV-SGSH), an adeno-associated virus (AAV) based gene therapy for Sanfilippo syndrome type A (MPS IIIA) and EB-101 (gene-corrected skin grafts) for recessive dystrophic epidermolysis bullosa (RDEB). • Abeona is also developing ABO-101 (AAV-NAGLU) for Sanfilippo syndrome type B (MPS IIIB), • ABO-201 (AAV-CLN3) gene therapy for juvenile Batten disease (JNCL), ABO-202 (AAV-CLN1) for treatment of infantile Batten disease (INCL), • EB-201 for epidermolysis bullosa (EB), • ABO-301 (AAV-FANCC) for Fanconi anemia (FA) disorder • ABO-302 using a novel CRISPR/Cas9-based gene editing approach to gene therapy for rare blood diseases. • In addition, Abeona has a proprietary vector platform, AIM™, for next generation product candidates.	• **João Siffert, MD** • **Interim Chief Executive** • Head of European Medical Affairs in October 2018, **Lykera Biomed and Digna Biotech,** where he spent more than 10 years leading teams dedicated to developing gene therapy • **Ph.D. in molecular biology from the University of Navarra.** He was a post-doctoral fellow at the University of Connecticut and earned his MBA from the IESE Business School at the University of Navarra.
Based	Cleveland, OH		
Ownership	**NASDAQ ABEO**		
Business Model	For Profit		
Valuation	Market Cap 12/20/2019 $159 M		
Financials	Total cash raised: $128.7 M		
Lead Product			
Product Type			
Stage	Ph. 1-2 (3 drugs)		
Indications			
website	www.abeonatherapeutics.com/		

Prevail Therapeutics

		Key Events	Key people
	2017	• Founded in a collaborative effort by Asa Abeliovich, M.D., Ph.D., OrbiMed and The Silverstein Foundation for Parkinson's with GBA, • Vision: to eradicate Parkinson's disease and related disorders. • they aim to translate recent advances in their understanding of the root genetic causes of these diseases into therapeutics for patients. • Through a partnership with REGENXBIO, they are utilizing the NAV AAV9 vector technology to advance a pipeline of gene therapy programs into therapies for patients in need.	• Asa Abeliovich is their Founder and Chief Executive Officer, bringing more than 25 years of academic and industry experience in research and the understanding of genetic and molecular mechanisms that underlie neurological disorders of aging, such as Parkinson's disease. • Prior to Prevail Therapeutics, Asa was Chief Innovation Officer and Co-Founder of Alector, a biotechnology company which is developing immune therapies for the treatment of neurodegenerative diseases. • Previously a tenured Associate Professor of Pathology, Cell Biology, and Neurology at Columbia University, as well as a member of the Taube Institute for Alzheimer's Disease and the Aging Brain. He has also previously served as an Attending Physician in Neurology at the New York-Presbyterian Hospital and the New York Psychiatric Institute. • 3 board members from OrbiMed VC
Based	New York, NY		
Ownership	**NASDAQ**		
Business Model	For Profit		
Valuation	Market Cap 12/20/2019 $548 M		
Financials	3/2018 Ser.. A $75 M OrbiMed 3/2019 Ser.. B $50 M		
Lead Product			
Product Type			
Stage			
Indications			
website	www.prevailtherapeutics.com		

GenSight Biologics S.A.

Founded	2011
Based	Paris, France
Ownership	IPO 7/2016 Paris exch. SIGHT **EPA SIGHT**
Business Model	For Profit
Valuation	Market Cap 12/20/2019 72.4M EURO
Financials	4/2013 Ser.. A €32 M Abingworth, Index Ventures, Novartis Venture Fund, Versant Ventures 7/2015 Ser.. B $36 M
Lead Product	GS010 for Leber Optic neuropathy
Product Type	
Stage	
Indications	
website	ensight-biologics.com

Key Events

- they are a clinical-stage biotechnology company discovering and developing novel therapies for mitochondrial and neurodegenerative diseases of the eye and central nervous system. To address these therapeutic areas, they leverage their integrated development platform by combining a gene therapy-based approach with their core technology platforms of mitochondrial targeting sequence, or MTS, and optogenetics.
- GS010 is an AAV2 gene therapy vector that encodes the human wild-type ND4 protein, which they are developing as a treatment of LHON caused by mutation of the ND4 gene. **GS010 for Leber Hereditary Optic Neuropathy (LHON) Phase 3**
- The ND4 gene is normally located in the mitochondria where ND4 proteins are synthesized. GS010 allows efficient allotopic expression of the mitochondrial gene ND4 in the nucleus thanks to a proprietary Mitochondrial Targeting Sequence that shuttles the messenger RNA from the nucleus directly to the outer membrane of the mitochondria. There, the ND4 proteins are synthesized and incorporated into the mitochondria. Wild-type ND4 proteins then integrate into Complex I of the respiratory chain and rescue the deficiency.
- **GS030 for Retinitis Pigmentosa.** The leading cause of hereditary blindness in developed countries, Retinitis Pigmentosa is characterized by progressive vision loss, for which there is currently no cure.
- **02/05/2019 announced that the Phase 3 study failed primary endpoint at 48 wks follow up**

Key People

- Bernard Gilly, Ph.D., one of their founders, has served as their Chief Executive Officer since their creation. From their creation through to 2016, Bernard served as Chairman of their Board of Directors.
- From 2011 through 2014, he served as Chief Executive Officer at Pixium Vision and from which date he has served as nonexecutive Chairman of the board of directors. In addition, he currently serves on the boards of Prophesee S.A. (formerly Chronocam) and Gecko Biomedical. From 2005 to 2009, he founded and was Chairman and Chief Executive Officer of Fovea Pharmaceuticals S.A., or Fovea, a privately funded company.

GenSight Pipeline

* Conducting this trial under a special protocol assessment with the FDA

Lysogene S.A.

		Key Events	Key People
Founded	2009	• LYSOGENE was founded in 2009, by Karen Aiach and Olivier Danos, with a focused scientific development plan, pragmatic approach and a bold mission. The company was built on a comprehensive understanding of the impact of neurodegenerative diseases on patients and families. • Lysogene has generated five non-cumulative years of clinical safety data to show the efficiency of a direct delivery route to the CNS with its initial gene therapy trial for MPS IIIA. Lysogene has recently completed the enrollment for the first multi-national observational study in MPS IIIA which will function as the non-concurrent control for the first pivotal trial for MPS IIIA in Q1 2018. Lysogene also plans a clinical trial for GM1 Gangliosidosis for 2019. Lysogene has obtained orphan drug designation from the EMA and FDA and rare pediatric designation by the FDA for both programs. • <u>MPS IIIA Phase I Pivotal Ph. 2-3 to start late 2018</u> • 10/2018: Long-term Follow-up of MPS IIIA Patients Treated by Intracerebral LYS SAF301 Gene Therapy licensing deal with Sarepta on US rights to gene therapy, LYS-SAF302, to treat Mucopolysaccharidosis type IIIA (MPS IIIA).	• Karen Aiach • **Founder, Chief Executive Officer** • Ms. Aiach is also the mother of a child with MPS IIIA. She has a strong business background starting her career with Arthur Andersen specializing in audit and transaction services. Her entrepreneurial experience includes founding and running a financial business consultancy. From 2008 to 2009, Ms. Aiach served as a Member of the Pediatric Committee at the European Medicines Agency (EMA), established in accordance with the European Pediatric Regulation, as a patient representative. In 2008, she also served on the French Ethical Review Board CCPPRB at Ambroise Paré Hospital.
Based	Paris, France		
Ownership	FR0013233475 / LYS Listed on: Euronext Stock Exchange **EPA LYS**		
Business Model	For Profit		
Valuation	Market Cap 112/20/9/2019 $23.2M		
Financials	5/2014 Ser.. A $22 M Sofinnova Investments		
Lead Product			
Product Type			
Stage	Phase 1		
Indications			
website	www.lysogene.com		

Freeline Therapeutics

		Key Events	Key People
Founded	2015	• 2010 • Professor Amit Nathwani, in collaboration with St. Jude Children's Research Hospital (Memphis, Tennessee), dosed his first hemophilia B patient using a gene therapy approach. This gene therapy showed very promising results with sustained long-term activity levels. • 2015 company founded by Professor Amit Nathwani, and collaborates with St Jude's • Adenovirus-Associated Virus Vector–Mediated Gene Transfer in Hemophilia B • Long-Term Safety and Efficacy of Factor IX Gene Therapy in Hemophilia B Ph. 1-2 • Pipeline includes lysosomal storage disorders • Targeting the liver with their novel gene therapy platform enables us to treat a wide range of chronic diseases. their unique split packaging technology and their high performing capsid allows us to target monogenic diseases and in the future treat complex disease areas not currently targeted by gene therapy. they will commercialize their next-generation AAV gene therapy platform for hemophilia B, while they continue to deploy the capsid and manufacturing platform across their pipeline of novel indications.	• **Anne Prener** • **Chief Executive Officer** • Anne brings to Freeline over 25 years of experience in drug development and executive leadership across several therapeutic areas, with special focus on rare diseases and gene therapy. • Anne most recently served as the CEO of Gyroscope Therapeutics, a preclinical gene therapy company focusing on ophthalmology, where she continues to serve as a non-executive Member of the Board. From 2014-2016, Anne was VP of Clinical Research Hematology and Global Therapeutic Area Head of Hematology in Baxalta, Boston, USA. • **MD from Copenhagen University** and holds a **PhD in Epidemiology**.
Based	UK and Germany		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials	Total cash raised: $155.9 M		
Lead Product			
Product Type			
Stage	Phase 1		
Indications			
website	www.lysogene.com		

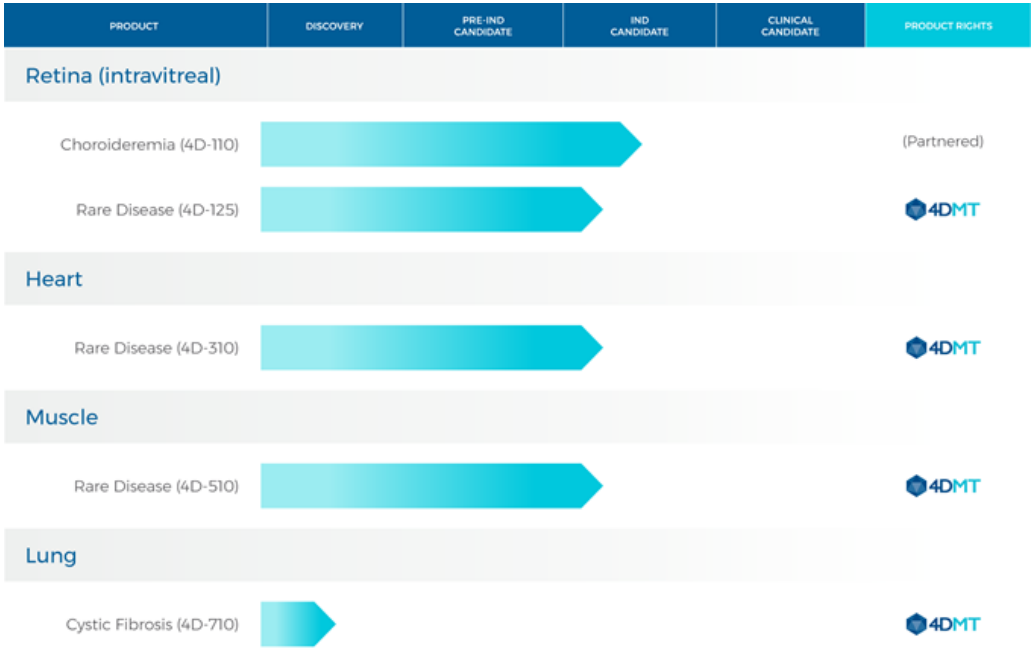
Generation Bio

		Key Events	Key People
Founded	2016	• their mission is to make the ravages of genetic diseases as imaginary to the next generation as polio and smallpox are for children. Co-founder and vice president, Robert Kotin, prev. with Voyager, scientist at NIH - developed using close-ended DNA (ceDNA) instead of viruses. ceDNA can move from the cytoplasm of the cell into the nucleus without a virus. It has been dubbed GeneWave technology, and the company believes it avoids the immune response that can be toxic in AAV-based gene therapy approaches. Provides durable, high levels of gene expression. This capsid-free technology enables repeated dosing and allows us to deliver transgenes of unprecedented size (>20 kb) . **Liver disorders** they are advancing a diverse portfolio of therapeutic candidates, formulated in lipid nanoparticles, for diseases of the liver. ▪ GSD1a, Glycogen storage disease type 1a (GSD1a); Hemophilia A; Progressive familial intrahepatic cholestasis (PFIC); PKU **Eye disorders**: Leber's congenital amaurosis; Stargard's disease	**GEOFF MCDONOUGH, MD** **President & Chief Executive Officer** Geoff formerly served as president and chief executive officer of Swedish Orphan Biovitrum AB (Sobi) from 2011 – 2017 Prior to Sobi, he held a variety of senior roles at Genzyme Corporation, including president of Genzyme Europe and senior vice president and general manager of the global lysosomal storage disease business. He obtained his **MD at Harvard Medical Schoo**l and completed his residency training in internal medicine and pediatrics at Massachusetts General Hospital and Boston Children's Hospital. Chairman BOD: Jason Rhodes is a partner at Atlas Venture.
Based	Cambridge, MA		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials	1/2018 Ser.. A $25 M Atlas Venture 2/2018 Ser.. B $100 M Fidelity Management and Research Company		
Lead Product	01/2020 Series C		
Product Type			
Stage			
Indications			
website	generationbio.com/		

4D Molecular Therapeutic

		Key Events	Key People
Founded	2013	• they create highly complex and unique vector capsid "libraries" for high-throughput screening. To date they have created over 30 unique AAV capsid libraries comprising more than an estimated 100 million novel variants. they therefore have roughly 10 million times more vectors to choose from than are used in 1st or 2nd generation AAV gene therapy products • NATURAL SELECTION IN VIVO: they use the power of natural selection to isolate the "most fit" vectors for any "Target Vector Profile" (TVP) they want. The TVP will define the cell types and intra-organ distribution to be targeted, the route of administration, the dosage required for delivery, and resistance to pre-existing antibodies in the population if desirable. • Once they have created and refined these highly optimized 4DMT AAV vectors, they then engineer them to carry a wide array of therapeutic transgene payloads for the treatment of diverse diseases, in addition to filing composition-of-matter patents and therapeutic use patents. • <u>PIPELINE SEE NEXT PAGE</u>	Prior to forming 4DMT, **their CEO David Kirn MD** and development team members have developed over 10 different therapeutic viral vectors, including translation into the clinic and Phase 1-3 clinical development in over 30 clinical trials.
Based	Emeryville, CA		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials	8/2015 Venture Round $7 M 9/2017 Venture Round $3 M Cystic Fibrosis Foundation 9/2018 Ser.. B $90 M Viking Global Investors		
Lead Product			
Product Type			
Stage			
Indications			
website	www.4dmoleculartherapeutics.com		

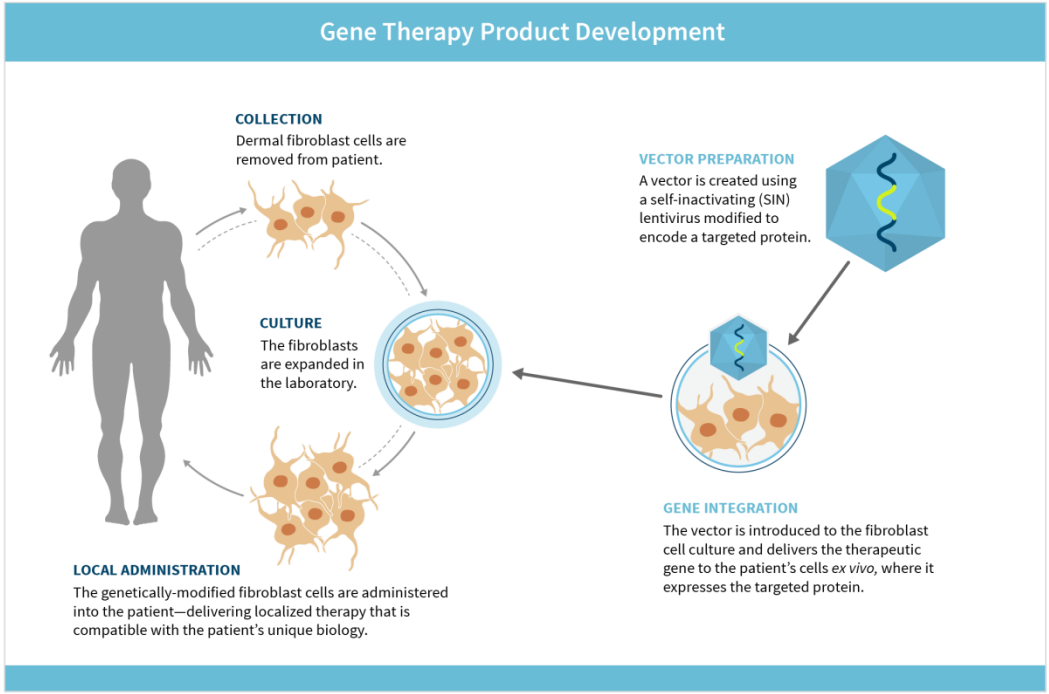
4D Molecular Ther. Pipeline



Fibrocell Science Inc

		Key Events	Key people
	1995	• Fibrocell Science, Inc. (NASDAQ: FCSC) is an autologous cell and gene therapy company 1. Autologous fibroblasts from skin biopsy and grown in the lab 2. A viral vector is created separately using "self Inactivated Lentivirus" encoded modified to encode a targeted protein 3. The vector is introduced in the fibroblast cell culture where it expresses the desirable protein 4. The genetically modified fibroblasts are the administered locally to e.g. the patient's skin • Translating personalized biologics into medical breakthroughs for diseases affecting the skin and connective tissue. Fibrocell's most advanced gene-therapy product candidate, FCX-007, has begun a Phase I/II trial for the treatment of recessive dystrophic epidermolysis bullosa (RDEB). • Fibrocell is in pre-clinical development of FCX-013, its gene-therapy product candidate for the treatment of linear scleroderma. In addition, Fibrocell has a third gene-therapy program in the research Phase: for the treatment of arthritis and related conditions. • Fibrocell's gene-therapy portfolio is being developed in collaboration with Intrexon Corporation (NYSE: XON), a leader in synthetic biology.{Also has an old platform for autologous fibroblasts}	• John Maslowski • **President and Chief Executive Officer** • Prior to that, he was Senior Vice President of Scientific Affairs, with oversight of research and development, clinical and regulatory affairs. Previously, he was Vice President of Operations with responsibility for manufacturing and quality operations. Prior to joining Fibrocell, Mr. Maslowski held various positions at Wyeth Pharmaceuticals, Inc. (now Pfizer, Inc.), eventually serving as Quality Assurance Manager. Prior to joining Wyeth, Mr. Maslowski held various positions with Merck & Co. and Teva. Mr. Maslowski earned a B.S. in Biology from the Ursinus College and an M.S. in Biology from Villanova University.
Based	Exton, PA		
Ownership	**NASDAQ FCSC**		
Business Model	For Profit		
Valuation	Market Cap 109/2019 $29.2M		
Financials	Total cash raised: $115 M		
Lead Product	See next column		
Product Type			
Stage			
Indications			
website	http://fibrocell.com/about/		

Fibrocell Gene Therapy



Fibrocell Pipeline

Program	Condition	Target	Research	Pre-Clinical	Phase 1/2 Clinical Trials	FDA Regulations
FCX-007	Recessive Dystrophic Epidermolysis Bullosa (RDEB)	Type VII Collagen				✓ Orphan Drug ✓ Rare Pediatric Disease ✓ Fast Track
FCX-013	Moderate to Severe Localized Scleroderma	MMP-1				✓ Orphan Drug ✓ Rare Pediatric Disease ✓ Fast Track
Research	Arthritis and Related Conditions	TBD				

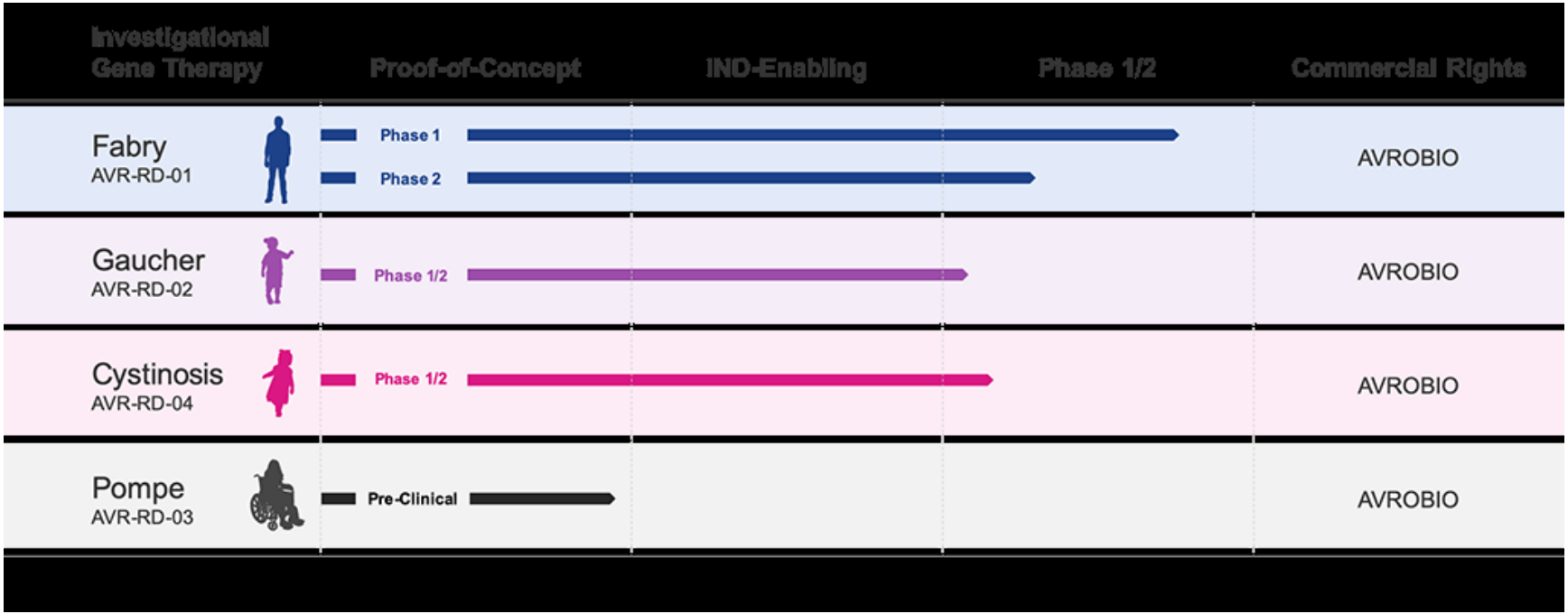
Passage Bio

		Key Events	Key people
Founded	2018	• Passage Bio is a fully integrated gene therapy company with a mission to develop a portfolio of five life-transforming AAV-delivered therapeutics for the treatment of rare monogenic central nervous system diseases , (gangliosidosis, and frontotemporal dementia. • Research, collaboration and license agreement with the University of Pennsylvania and its Gene Therapy Program (GTP) as well as the Orphan Disease Center (ODC). • Pursuant to the research collaboration, GTP conducts IND-enabling preclinical work, and Passage Bio is responsible for clinical development, regulatory, manufacturing and commercialization of all product candidates. The ODC is responsible for natural history studies, KOL engagement, and patient advocacy outreach. • Partnering with U of Penn on preclinical work and with Paragon on manufacturing	• Founder james Wilson • CEO Stephen Squinto, Ph.D. is a Venture Partner at OrbiMed Advisors who brings over 25 years of biotechnology industry experience to Passage Bio. • Dr. Squinto was a co-founder of Alexion Pharmaceuticals Inc. and recently served as its Executive Vice President and Chief Global Operations Officer. Alexion, Dr. Squinto was involved in the discovery, development and commercialization of Soliris, one of the world's most successful orphan drug products for patients across several rare, life-threatening diseases.
Based	Philadelphia, PA		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials	225.5 M raised Ser. A (110M) and B (125M)		
Lead Product			
Product Type	AAV based		
Stage	Early*		
Indications	CNS		
website	Passagebio.com		

AVRO Bio Inc

		Key Events	Key people
Founded	2015	• AVROBIO, Inc., a leader in lentiviral-based gene therapies, • is a clinical stage company developing disruptive therapies that have the potential to transform patients' lives in a single dose	**Geoff MacKay,** President & CEO • Prev. CEO of Organogenesis Inc., the company treated 1 million patients with living cell therapies, received the first FDA CBER allogeneic cell-therapy approval and achieved an unparalleled position within regenerative medicine. • Founding CEO of eGenesis, applying CRISPR Cas-9 gene editing to xenotransplantation. • 11 years at Novartis in senior leadership positions Past Chairman of the Board of A;;iance of Regenmerative medicine (ARM). **Birgitte Volck, MD, PhD ,** President of Research & Development, • prev. Senior Vice President and Head of R&D, Rare Disease at GSK in the UK, CM) and SVP, Head of Development at Swedish Orphan Biovitrum (SOBI)
Based	Cambridge, ma		
Ownership	**NASDAQ AVRO**		
Business Model	For Profit		
Valuation	622M Jan 11 2020		
Financials	IPO 6/2018 raised 99M		
Lead Product	2020/02/19: Announces follow on public offering $100M		
Product Type	Lenti-viral based gene therapy		
Stage			
Indications			
website	Avrobio.com		

AVRO BIO PIPELINE



Meira GTX Holdings plc

		Key Events	Key people
Founded		• cCinical-stage gene therapy company focused on developing potentially curative treatments for patients living with serious diseases. • We currently have six programs in clinical development including four ocular indications, a salivary gland condition, and a Parkinson's disease program. • Our initial focus on diseases of the eye, salivary gland and central nervous system is based on the significant unmet medical need coupled with the high potential gene therapy has to provide meaningful clinical benefit in these areas. • AAV vector is manufactured in 20,000 sqf state-of-the-art manufacturing facility, completed in early 2018. • We currently have six programs in clinical development, including Phase 1/2 clinical stage programs in Achromatopsia (ACHM), X-Linked Retinitis Pigmentosa (XLRP) and RPE65-Deficiency, a Phase 1 program and a second Phase 1/2 trial clinical trial in radiation-induced xerostomia (RIX) and a Parkinson's program that has completed a Phase 2 trial with published data.	**Dr. Alexandria Forbes President, CEO Executive Officer** • Prev. served as Senior VP Commercial Operations at Kadmon Holdings, Inc., • Prev. healthcare investor at Sivik Global Healthcare, and Meadowvale Asset Management, • Prev. Human Frontiers/Howard Hughes postdoctoral fellow at the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center and research fellow at Duke University, and also at the Carnegie Institute at Johns Hopkins University. • Dr. Forbes received an M.A. in Natural Sciences from Cambridge University and a Ph.D. in molecular biology from Oxford University
Based	New York NY, London UK		
Ownership			
Business Model	For Profit		
Valuation	IPO 6/2018 raised 75M Market cap 719M 1/10 2020		
Financials			
Lead Product			
Product Type	AAV based treatments of rare disorders		
Stage			
Indications			
website	Meiragtx.com		

Tocagen Pharmaceuticals Inc

		Key Events	Key people
Founded	2007	• At the core of our approach is a cancer-selective gene therapy platform that utilizes retroviral replicating vectors (RRVs), which are designed to deliver therapeutic genes into the DNA of cancer cells. RRV-mediated gene delivery fights cancer through a combination of mechanisms without the autoimmune toxicities that patients commonly experience with other treatments. • RRVs are designed to selectively integrate into the DNA of cancer cells, which then serve as factories to produce more RRVs by budding. These progeny RRVs infect neighboring cancer cells, providing long-term presence of the therapeutic gene or genes. • RRV have the potential to selectively infect cancer cells to stimulate robust and durable anti-cancer immune responses, and can do so with minimal toxicity. **Two compomnent treatment"** • **TOCA 511= retroviral vector** **TOCA FC =slow release prodrug for 5FU** • Glioblastoma Ph 3	Marty J. Duvall CEO, since2016. • He holds over 30 years of oncology drug development and commercialization experience, executive vice president, chief commercial officer of ARIAD Pharmaceuticals, Inc., general manager for the oncology franchise at Merck & Co., Inc., Abraxis Bioscience, Inc., cquired by Celgene; and MGI Pharma, Inc acquired by ESAI.
Based	San Diego		
Ownership	**NASDAQ TOCA**		
Business Model	For Profit		
Valuation	99M 1/10/2020		
Financials	IPO 2017 raised 85M		
Lead Product			
Product Type			
Stage	Clinical Ph 3		
Indications	Glioma blastoma		
website	Tocagen.com		

Solid Biosceinces Inc

		Key Events	Key people
Founded	2013	• Focus on muscle dystrophy: Mechanism In Duchenne, the absence or near-absence of the protein dystrophin leads to muscle membrane instability and disruption of the dystrophin glycoprotein complex (DGC). Microdystrophin is a synthetic version of the dystrophin gene that is believed to retain its key components and functionality. In preclinical models, therapeutic administration of microdystrophin by adeno-associated virus (AAV) has been shown to stabilize the DGC and restore muscle function. • Impact on Duchenne The large size of the dystrophin gene has historically prevented direct replacement as a therapeutic strategy. Preclinical studies have shown that microdystrophin AAV-mediated gene transfer enables systemic delivery of the truncated gene and has the potential to slow or halt disease progression, regardless of the type of dystrophin gene mutation.	**Ilan Ganot** started Solid in 2013 to find treatments, and potentially a cure, for Duchenne muscular dystrophy, a disease that afflicts his son Eytani. • Prior to starting Solid, Mr. Ganot was an investment banker at JPMorgan Chase in London, specializing in hedge fund driven equities business for the firm. • Also worked at Nomura Securities in London, Hong Kong and New York, where he managed relationships with investors and clients of the firm. • Prior to Nomura, Mr. Ganot was a senior salesperson for Lehman Brothers' European Equities business. • Prev. practicedlaw at the Israeli law-firm, Haim Zadok & Co, where his focus was private equity law and mergers and acquisitions. • MBA from London Business School and holds law and business degrees from the IDC in Herzliya, Israel.
Based	Cambridge, MA		
Ownership	**NASDAQ SLDB**		
Business Model	For Profit		
Valuation	IPO 1/2018 raised 125M M arket cap 1/10/2020 165M		
Financials			
Lead Product			
Product Type	AAV base gene therapy		
Stage	Phase 1		
Indications			
website	Solidbio.com		

GENE EDITING COMPANIES

Bluebird Bio

	1992
Based	Cambridge, MA
Ownership	**NASDAQ BLUE**
Business Model	For Profit
Valuation	At IPO 6/2013 $389 M arket CMap 12/20/2019 $4.9 B
Financials	6/2004 Ser.. A $8.5 M 10/2004 Venture Round $12 M Techno Venture Management 3/2010 Ser.. B $35 M Sanofi-Genzyme BioVentures, Third Rock Ventures 4/2011 Venture Round $30 M ARCH Venture Partners 7/2012 Ser.. D $60 M 10/2012 Venture Round $9.3 M California Institute for Regenerative Medicine IPO 6/2013 raised $116.1 M
website	www.bluebirdbio.com

Key Events

- Founded by Phillippe Leboulch
- Bluebird bio is developing potentially transformative gene therapies for severe genetic diseases.
- The company's platform treats the cause of genetic diseases by placing a healthy gene into the patient's extracted bone marrow stem cells, and transplanting these corrected stem cells back into the patient
- At the heart of bluebird bio's product creation efforts is its broadly applicable gene therapy platform for the development of novel treatments for diseases with few or no clinical options. Bluebird bio's approach represents the ultimate personalized therapy and a true paradigm shift in the treatment of severe genetic diseases by presenting a potential one-time transformative option for patients.
- Bluebird bio has three clinical-stage programs in development :
  - Childhood cerebral adrenoleukodystrophy (CCALD) Ph. 2-3
  - Betathalassemia/sickle cell disease. Ph. 1-2
  - Multiple myeloma Ph. 1-2
- Led by a world-class team, bluebird bio is privately held and backed by top-tier life sciences investors.
- **2019/06/03 European Medicines Agency (EMA) approved Zynteglo for patients with transfusion dependent Betha Thalassemia. Launched delayed to 2020 due to manufacturing issues Expected ptice 315,000 Euro/year for 5 years2020/02/19: Reay for launch in first half or 2020**

Kkey people

- Nick Leschly has served as chief bluebird since September 2010.
- Formerly, Nick was a partner and founding member of Third Rock Ventures in 2007.
- Nick played an integral role in the overall formation, development and business strategy of several of Third Rock's portfolio companies, including Agios Pharmaceuticals, Inc. and Edimer Pharmaceuticals, Inc.
- Prior to joining Third Rock, he worked at Millennium Pharmaceuticals, leading several early-stage drug development programs and served as the product leader for VELCADE.
- Nick also founded and served as chief executive officer of MedXtend Corporation.
- He received his B.S. in molecular biology from Princeton University and his **MBA from Wharton Business School**

ElevateBio

		Key Events	Kkey people
	2019	• *Creating and operating a portfolio of cell and gene therapy companies to develop, manufacture and commercialize life-transforming medicines*	• Co-founders David Hallal, CEO and Chairman, Executive Paartner MPM Capital ➢ Prev CEO of Alexion and 30 years in biotech incl. Eytech, Biogen and Amgen. • Co-founder Mitchell H. Finer, PhD, President & CSO, globally recognized pioneer in cell and gene therapies, former CSO BlueBird and CEO in many companies. and MPM portfolio companies. ➢ He founded and is the former CEO of Oncorus, focused on the development of oncolytic herpes viruses for the treatment of solid tumors. ➢ He is also a founder and the former CEO of CODA Biotherapeutics, focused on developing a chemogenetic neuromodulation platform for the treatment of severe neurological disorders..
Based	Cambridge, MA		
Ownership	**Private**		
Business Model	For Profit	• *A biotechnology holding company, established to create and operate a broad portfolio of cell and gene therapy companies through partnerships with leading academic researchers, medical centers and entrepreneurs. ElevateBio builds single- and multi-product companies by providing scientific founders with fully-integrated bench-to- bedside capabilities including world-class scientists, manufacturing facilities, drug developers and commercial expertise. ElevateBio is building a team of industry leaders who work at the holding company and are assigned exclusively or in-part to ElevateBio portfolio companies over time. ElevateBio BaseCamp, a company-owned Center of Cell and Gene Therapy Innovation, will serve as the R&D, process development and manufacturing hub across the entire ElevateBio portfolio while also supporting selected strategic partners.*	
Valuation			
Financials	5/2019 Ser.. A $150 M Investors include UBS Oncology Impact Fund; MPM Capital; F2Ventures; Samsara BioCapital; Redmile Group;EcoR1Capital		
website	elevateBio.com		
		• "Many Companies – One Robust Organization"	
		• ElevateBio's novel business model, including BaseCamp, our centralized R&D and manufacturing organization, is structured to rapidly and efficiently build single- and multi-product cell and gene therapy companies.	

Sangamo Therapeutics

		Key Events	Kkey people
	1995	• ***PIONEERING GENETIC CURES*** t- leader in the development of a proprietary technology platform that enables specific regulation of gene expression and gene modification. • The basis of this platform is a naturally occurring class of transcription factors, zinc finger DNA-binding proteins (ZFPs) which they can engineer to drive desired therapeutic outcomes. • Engineered ZFPs can be linked to functional domains that normally activate or repress gene expression to create ZFP transcription factors (ZFP TFs) capable of turning genes on or off. <u>they can also link ZFPs to nuclease domains to create zinc finger nucleases (ZFNs) which enable precise gene-editing in cells.</u> • Engineered ZFNs can modify a cell's DNA at a precise location, thereby facilitating correction or disruption of a specific gene or the targeted addition of a new DNA sequence. "their primary mission is to develop ZFP Therapeutics®. they have ongoing clinical programs to evaluate ZFP TFs and ZFNs as novel approaches to unmet medical needs where they believe they have a differential technical advantage to impact the outcome of disease by functioning at the DNA level." • MPS I and MPS II : Phase 1- • **<u>02/08/2019 MPS II study failed to show benefit in first 6 patients –trying higher</u> dose but stock dropped 30%** • Hemophilia B: In Phase 1-2 SEE NEXT PAGE	• Founding CEO was Edward Lampier, the inventor of gene expression regulation based on "zinc-finger nuclease" gene editing technology • SANDY MACRAE, M.B., CH.B., Ph.D. Chief Executive Officer since June 2016. • Global Medical Officer of Takeda Pharmaceuticals. • From 2001 to 2012, Dr. Macrae held roles of increasing responsibility at GlaxoSmithKline, including Senior Vice President, Emerging Markets Research and Development (R&D), from 2009 to 2012. • Dr. Macrae received his B.S. in Pharmacology and his M.B., Ch.B. with honors from Glasgow University. He is a member of the Royal College of Physicians. Dr. Macrae also earned his Ph.D. in molecular genomics at King's College, Cambridge.
Based	Richmond, CA		
Ownership	**NASDAQ SGMO**		
Business Model	For Profit		
Valuation	Market Cap 12/20/2019 $975M		
Financials	Total cash raised: $93.2 M		
Lead Product	See pipeline next page		
Product Type			
Stage			
Indications			
website	www.sangamo.com		

Sangamo Partnered Pipeline

- Hemophilia A Ph. 1-2 (Novartis)
- Betha Thalassemia Ph. 1-2 (Bioverativ)
- Sickle Cell –Preclin. (Bioverative)
- ALS/FTLD –Prelin. (Pfizer)
- Huntingtons –Research (Shire)

- Oncology (Kite/Gilead)
- HIV T-Cells –Ph. 1-2
- HIV -Stem cells –Ph. 1-2

Moderna Therapeutics (1)

		Key Events	Kkey people
	2010	***Mission:***	• Patrick Rossi, Tim Springer from Harvard, Bob Langer from MIT, Noubar Afevan from Flagship Ventures
Based	Cambridge, MA 735 employees	• ***Deliver on the promise of mRNA science to create a new generation of transformative medicines for patients.***	• Stepanie Barcel CEO of BIOMerieux (DIAGNOSTICS) recruited to become CEO.
Ownership	**NASAQ MRNA**	• Moderna was founded in 2010 and the name was originally written "ModeRNA".	
Business Model	For Profit	• At Moderna, they are pioneering the development of a new class of drugs made of messenger RNA (mRNA). This novel drug platform builds on the discovery that modified mRNA can direct the body's cellular machinery to produce nearly any protein of interest, from native proteins to antibodies and other entirely novel protein constructs that can have therapeutic activity,	
Valuation	At IPO 12/2018 $7.6 B Market Cap 12/20/2019 $5.6 B	• In 2012, they had raised $40 million from Flagship Ventures' VentureLabs unit and other private investors	
Financials	Total cash raised: $1.8 B IPO 12/2018 raised $604 M	• 2013, DARPA award up to $24.6 M to fight infectious diseases and biological weapons.	
Lead Product	21 products, 11 in clinical Phase	• 2014, deal w Alexion Pharmaceuticals entered a $125 million deal for orphan diseases. Alexion paid Moderna $100 million exchange for 10 product options to develop rare-disease drugs. [A year later Moderna launched its own venture, Epidera, for Rare diseases	
Product Type	infectious Diseases Immuno-Oncology Rare Diseases	• SEE NEXT PAGE	
Stage			
website	www.modernatx.com/		

Moderna Therapeutics (2)

		Key Events	Kkey people
	2010	• 2014, research and clinical partnership with Karolinska Institutet and Karolinska University Hospital, and established Moderna Therapeutics Sweden • Deals with AstraZeneca (immuno oncology), Merck (vaccines), Vertex (Cystic Fibrosis) - September 2016, Moderna announced that it was going to start building a 200,000 sq ft GMP mRNA manufacturing facility in Norwood, MA. • In 2017 Science published an article describing Moderna's platform, which was the result of several months of discussions with Moderna employees. Moderna had made the strategic decision to disclose some of its approach in an effort to break the hype cycle into which it was getting locked.[32] The Science piece disclosed that Moderna was delivering some of its mRNA therapeutic candidates in liposomes, that they were using modified uridine nucleosides based on work done by Katalin Karikó on avoiding immune responses to mRNA drugs, that the company was using mRNAs with modified sequences to improve folding and translation efficiency, and that their mRNA drug candidates were modified on each end, outside the coding region, to target them to specific cell types.	
Based			
Ownership			
Business Model			
Valuation			
Financials			
Lead Product			
Product Type			
Stage			
website			

Translate Bio

Founded	2011
Based	Lexington, MA
Ownership	**NASDAQ TBIO**
Business Model	For Profit
Valuation	At IPO 6/2018 $582 M Market Cap 12/20/2019 $506 M
Financials	11/2011 Venture Round $2.7 M 1/2012 Ser.. A $20.7 M Atlas Venture 7/2015 Ser.. B $63.8 M MRL Ventures Fund 1/2017 Ser.. C $51 M IPO 6/2018 raised $122 M
Lead Product	Cystic Fibrosis
Product Type	MRTTM platform
Stage	Clinical
Indications	
website	https://translate.bio/

Key Events

- A leading mRNA therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction. Using proprietary mRNA therapeutic platform (MRTTM), the company is creating RNA that encodes functional proteins. mRNA is delivered to the target cell where the cell's own machinery recognizes it and translates it, restoring or augmenting protein function to treat or prevent disease.
- The MRTTM platform has been in development for the past ten years, initially at Shire and internally at Translate since 2016. With the scientific founders of MRTTM now part of the leadership team, they have built on Shire's initial pioneering work and investment to advance the goal of bringing a transformative mRNA approach to patients.
- "they believe that their MRTTM platform is applicable to a broad range of diseases caused by insufficient protein production or where production of proteins can modify disease, including diseases that affect the lung, liver, eye, central nervous system, lymphatic system and circulatory system. their two lead programs are being developed as treatments" for cystic fibrosis (CF) and ornithine transcarbamylase (OTC) deficiency.

Key People

- Ronald C. Renaud, Jr.
- Chief Executive Officer
- since 2014. Formerly, t Idenix Pharmaceuticals (2007-2014), where he served as chief financial officer, chief business officer and finally, president and chief executive officer.
- Under his leadership, Idenix refocused its drug-discovery and development efforts and which culminated in its acquisition by Merck for $3.85 billion in August 2014.
- Prev. he was a biotechnology equity research analyst at J.P. Morgan, Schwab Soundview and Bear Stearns.

Caribou Biosciences, Inc (1)

		Key Events	Key people
	2011	• Caribou was founded by James Berger, Jennifer Doudna, Martin Jinek, and Rac el Haurwitz, scientists from the U. California, Berkeley based on the remarkable nucleic acid modification capabilities found in prokaryotic CRISPR systems. • Caribou Biosciences is a biotechnology company in genome engineering. they develop technology-based solutions for cellular engineering and analysis based on the CRISPR-Cas9 technology platform. Cas9, when paired with a guide RNA, cuts double-stranded DNA allowing for specific changes to DNA. These site-specific DNA modifications can be utilized to carry out sophisticated gene knock-outs or knock-ins. • In 2007, Rodolphe Barrangou, a former Chairman of the Board of Directors of Caribou Biosciences and current scientific advisor, led the group that characterized CRISPR systems as a form of prokaryotic adaptive immunity that provides a critical line of defense against invading phages, plasmids, and environmental nucleic acids. CRISPR systems have evolved to enable prokaryotes to acquire DNA from their environment and incorporate it into their genomes within specialized arrays of repetitive DNA. These CRISPR sequences act as a form of prokaryotic adaptive immunity that provides a critical line of defense against invading phages, plasmids, and environmental nucleic acids. CRISPR systems have evolved to enable prokaryotes to acquire DNA from their environment and incorporate it into their genomes within specialized arrays of repetitive DNA. **CONTIUES NEXT PAGE**	• Rachel Haurwitz, Ph.D. • President and Chief Executive Officer • Rachel is a co-founder of Caribou Biosciences and has been President and CEO since its inception in 2011. • She has a research background in CRISPR-Cas biology • Co-founder of Intellia Therapeutics. • 2014, she was named by Forbes Magazine to the "30 Under 30" list in Science and Healthcare, and in 2016, Fortune Magazine named her to the "40 Under 40" list of the most influential young people in business. • In 2018, the Association for Women in Science recognized Rachel with the annual Next Generation Award. • Inventor on several patents and patent applications covering multiple CRISPR-based technologies,
Based	Berkeley, CA		
Ownership	**Private**		
Business Model	For Profit		
Valuation			
Financials	Total cash raised: $74.6 M		
Lead Product			
Product Type	CRISP		
website	cariboubiosciences.com		

Caribou Biosciences, Inc (2)

		Key Events	Key people
	2011	• These CRISPR sequences act as a form of genomic memory that can be accessed to defend the cell when it is invaded by plasmids or phages that contain the recorded sequences. • At the core of Caribou's extensive CRISPR technology IP portfolio is an exclusive license to the foundational CRISPR-Cas9 work from the University of California and the University of Vienna. Caribou licenses this technology to strategic partners who are recognized leaders in the target market sectors. • 09/2018: ZUG, Switzerland, CAMBRIDGE, Mass., and BERKELEY, Calif. Sept. 10, 2018 -- CRISPR Therapeutics AG (NASDAQ:CRSP), Intellia Therapeutics, Inc. (NASDAQ:NTLA) and Caribou Biosciences, Inc. announced that the U.S. Court of Appeals for the Federal Circuit (the "Federal Circuit") affirmed the decision by the U.S. Patent and Trademark Office's ("USPTO") Patent Trial and Appeal Board ("PTAB") in an interference proceeding relating to CRISPR/Cas9 genome editing technology. The interference was requested by the Regents of the University of California, the University of Vienna and Dr. Emmanuelle Charpentier (collectively "UC"), co-owners of foundational intellectual property relating to CRISPR/Cas9 genome engineering, against the Broad Institute, Harvard University and the Massachusetts Institute of Technology (collectively "Broad") • The USPTO recently issued U.S. Patent No. 10,000,772 for the use of CRISPR/Cas9 genome editing covering widely used guide formats in various environments, including eukaryotic cells. The companies expect this is the first of many patents that will issue based on the foundational work done by Drs. Charpentier and	•
Based			
Ownership			
Business Model			
Valuation			
Financials			
Lead Product			
Product Type			
Stage			
website			

CRISPR Therapeutics

		Key Events	Key people
	2013	• Founded by Prof Roger Novak , Vienna, prof Emmanuelle Charpentier and Shaun Foy CRISPR Therapeutics is focused on the development of transformative medicines using its proprietary CRISPR/Cas9 gene-editing platform. CRISPR/Cas9 is a revolutionary technology that allows for precise, directed changes to genomic DNA. They have licensed the foundational CRISPR/Cas9 patent estate for human therapeutic use from their scientific founder, Dr. Emmanuelle Charpentier, Max Planck Institute in Germany [and previously Umea University, Sweden -filing patent with Jennifer Doudna, UC Berkeley, upheld in appeals court 2018], who co-invented the application of CRISPR/Cas9 for gene editing. Their multi-disciplinary team of world-class researchers and drug developers is working to translate CRISPR/Cas9 technology into breakthrough human therapeutics. **For latest update on patent litigation: https://www.broadinstitute.org/crispr/journalists-statement-and-background-crispr-patent-process**	• Dr. Samarth Kulkarni has served as Chief Executive Officer since December 2017. • Prev. CBO • Prev/ Partner at McKinsey & Company, where he had a leading role in the Pharmaceutical • Ph.D. in Bioengineering and Nanotechnology from the University of Washington and a B. Tech. from the Indian Institute of Technology
Based	Cambridge, MA		
Ownership	**NASDAQ CRSP**		
Business Model	For Profit		
Valuation	At IPO 10/2016 $590.4 M Market Cap 12/20/2019 $3.8 B		
Financials	4/2014 Ser.. A $25 M Versant Ventures 4/2015 Ser.. A $35 M Celgene, SR One 4/2015 Ser.. B $29 M Celgene, SR One 6/2016 Ser.. B $38 M Franklin Templeton Investments, New Leaf Venture Partners IPO 10/2016 raised $56 M **Public Offering announced 11/20/2019:**	• β-thalassemia and sickle cell disease will soon enter clinical testing. • Allogeneic CAR-T cell therapies to treat cancers, offers potential therapeutic advantages over the current generation of therapies. • 9 projects, incl. 1 entering Phase 1 in hemoglobinopathies (Beta Thalassemia and Sickle Cell), partnered with Vertex since 2015 • Other programs in immuno-oncology, genetic diseases, muscular dystrophy, etc. • J-V with Bayer Casebia Therapeutics to bring breakthrough therapies to patients suffering from serious conditions such as blood disorders, blindness and congenital heart disease.	
Indications	S		
Website	http://www.crisprtx.com		

Vertex Therapeutics

		Key Events	Key people
	2013	• Founded by Prof Roger Novak , Vienna, prof Emmanuelle Charpentier and Shaun Foy CRISPR Therapeutics is focused on the development of transformative medicines using its proprietary CRISPR/Cas9 gene-editing platform. CRISPR/Cas9 is a revolutionary technology that allows for precise, directed changes to genomic DNA. They have licensed the foundational CRISPR/Cas9 patent estate for human therapeutic use from their scientific founder, Dr. Emmanuelle Charpentier, Max Planck Institute in Germany [and previously Umea University, Sweden -filing patent with Jennifer Doudna, UC Berkeley, upheld in appeals court 2018], who co-invented the application of CRISPR/Cas9 for gene editing. Their multi-disciplinary team of world-class researchers and drug developers is working to translate CRISPR/Cas9 technology into breakthrough human therapeutics. • β-thalassemia and sickle cell disease will soon enter clinical testing. • Allogeneic CAR-T cell therapies to treat cancers, offers potential therapeutic advantages over the current generation of therapies. • 9 projects, incl. 1 entering Phase 1 in hemoglobinopathies (Beta Thalassemia and Sickle Cell), • Other programs in immuno-oncology, genetic diseases, muscular dystrophy, etc. • J-V with Bayer Casebia Therapeutics to bring breakthrough therapies to patients suffering from serious conditions such as blood disorders, blindness and congenital heart disease. • Oct 21/2019 rikafta is approved by the FDAtients with cystic fibrosis.	• Dr. Samarth Kulkarni has served as Chief Executive Officer since December 2017. • Prev. CBO • Prev/ Partner at McKinsey & Company, where he had a leading role in the Pharmaceutical • Ph.D. in Bioengineering and Nanotechnology from the University of Washington and a B. Tech. from the Indian Institute of Technology
Based	Cambridge, MA		
Ownership	**NASDAQ VRTX**		
Business Model	For Profit		
Valuation	At IPO 10/2016 $590.4 M **Market Cap 12/20/2019 $ 56.75B**		
Financials	4/2014 Ser.. A $25 M Versant Ventures ;4/2015 Ser.. A $35 M Celgene, SR One; 4/2015 Ser.. B $29 M Celgene, SR ne 6/2016 Ser.. B $38 M Franklin Templeton Investments, New Leaf Venture PartnersIPO 10/2016 raised $56 M		
Lead Product	**Trikafta approved for cystic fibrosis Oct 21, 2019**		
Product Type			
Website	Vrtx.com		

Trikafta Approval Cystic Fibrosis

- Trikafta is a combination of three drugs (elexacaftor, tezacaftor and ivacaftor tablets; ivacaftor tablets), co-packaged for oral use , that target the defective CFTR protein. It helps the protein made by the CFTR gene mutation function more effectively.
- Currently available therapies that target the defective protein are treatment options for some patients with cystic fibrosis, but many patients have mutations that are ineligible for previuos treatment options.
- Trikafta is the first approved treatment that is effective for cystic fibrosis patients 12 years and older with at least one F508del mutation, which affects 90% of the population with cystic fibrosis or roughly 27,000 people in the United States.
- Annual treatment cost 311,000 USD/ annually. It is not defined as a gene therapy , is not curative and must be taken twice daily.

Casebia, Inc

		Key Events	Key people
	2016	• Launched with a $300 million financial commitment, Casebia is well-positioned to achieve its goals by tapping the considerable scientific and financial resources of its joint venture partners, Bayer and CRISPR Therapeutics • Casebia is a private, independent company focused on discovering and developing CRISPR/Cas9 therapeutics to treat the genetic causes of bleeding disorders, autoimmune disease, blindness, hearing loss and heart disease. A strong foundation – comprised of a large up-front financial commitment combined with a license to the foundational CRISPR/Cas9 patent estate. • Current programs include treatments for Hemophilia A, Severe Combined Immunodeficiencies (SCID), Immunodysregulation Polyendocrinopathy Enteropathy X-Linked Syndrome (IPEX) and several ophthalmological diseases. • PIPELINE SEE NEXT SLIDE	• Jim Burns is President and CEO 25 years at Sanofi-Genzyme. First joining Genzyme in 1986, he advanced in multiple leadership roles to become Head of Sanofi's North American R&D Hub, where he was responsible for coordinating R&D operations across key therapeutic areas. • Doctorate in Bioengineering from the University of Illinois-Chicago, where his thesis work focused on drug delivery. Following his graduate studies, Burns was a post-doctoral researcher at the University of Florida. • Elected to the National Academies' National Academy of Engineering in 2010.
Based	Cambridge, MA and SF, CA		
Ownership	**J-V between CRISPR and Bayer** **Private**		
Business Model	For Profit		
Valuation			
Financials			
Lead Product	See next page		
Product Type			
Stage	Clinical		
website	casebia.com/		

Casebia Pipeline

	Platform	Programs	Status
		HEMATOLOGY	
in vivo	Liver	Hemophilia A	Research
		Undisclosed	Research
ex vivo	CD34+	Severe Combined Immunodeficiency (SCID)	Research
		Undisclosed	Discovery
		AUTOIMMUNE	
ex vivo	T cell	*Immunodysregulation polyendocrinopathy X-linked syndrome (IPEX)	Research
		Undisclosed	Discovery
		OPHTHALMOLOGY	
in vivo	Retina	Undisclosed	Research
		Undisclosed	Research
		Undisclosed	Research
		CARDIOVASCULAR	
		Undisclosed	Discovery

*Collaboration with Seattle Children's Research Institute

Intellia Therapeutics

		Key Events	Key people
	2014	• There are two main components to the CRISPR/Cas9 genome editing system: The Cas9 protein, which initially recognizes the DNA and also acts like a pair of "molecular scissors" that precisely cleave the targeted DNA sequence and The guide RNA, which recognizes the specific target DNA sequence, allowing the Cas9 scissors to cut. • 5/2018: Intellia announced that its first cell therapy target is WT1 for the treatment of acute myeloid leukemia and other potential hematological malignancies, as well as for solid tumors. • 12/2018 collaboration agreement w Novartis, 10M upfront: Under the terms of the original agreement, Novartis received exclusive rights to develop all collaboration programs focused on engineered chimeric antigen receptor T cells (CARTs), while both companies committed to advancing their respective hematopoietic stem cell (HSC) programs. The work of these preclinical programs, including for sickle cell disease, is ongoing. • 6/2018 CRISPR Therapeutics (NASDAQ:CRSP), Intellia Therapeutics, Inc. (NASDAQ:NTLA), and Caribou Biosciences, Inc., announced that The Regents of the University of California, the University of Vienna and Emmanuelle Charpentier, Ph.D. (collectively, "UC"), co-owners of foundational intellectual property relating to CRISPR/Cas9 genome editing technology, were granted U.S. Patent No. 10,000,772 ("the '772 patent") today by the U.S. Patent and Trademark Office (USPTO).	• 2017: John Leonard, M.D. • President and Chief Executive Officer • After a 30-year career in Pharmaceutical R&D, John Leonard retired from his position as Chief Scientific Officer and Senior Vice President of Research and Development at AbbVie in 2013. Inspired by the opportunity to work with a new therapeutic modality and form a new company, he returned to his life's passion and joined the Intellia team to direct the research and development effort to make CRISPR/Cas9 technology into a therapeutic reality.
Based	Cambridge, MA		
Ownership	**NASDAQ NTLA**		
Business Model	For Profit		
Valuation	At IPO 5/2016 $772.1 M Market Cap 12/20/2019 $689.9 M		
Financials	11/2014 Ser.. A $15 M Atlas Venture, Novartis 9/2015 Ser.. B $70 M OrbiMed IPO 5/2016 raised $108 M		
Lead Product			
Product Type			
Stage	Preclin. AML		
website	r.intelliatx.com		

Orchard Therapeutics plc

Founded	2015
Based	London, UK, Boston, MA, SF CA
Ownership	**NASDAQ: ORTX**
Business Model	For Profit
Valuation	1.5B
Financials	IPO 2018 raised 822M (eval at IPO 1.2B) / Ser A,B,C raised 310.5M
Lead Product	Strimvelis®
Product Type	autologous ex vivo gene therapy
Stage	Commercial
website	www.orchard-tx.com

Key Events

- Orchard Therapeutics is a leading global fully integrated commercial-stage company dedicated to transforming the lives of patients with rare diseases through innovative gene therapies.
- Orchard's portfolio of autologous ex vivo gene therapy programs has demonstrated sustained clinical benefit in over 150 patients across five disease areas. These programs include Strimvelis®, the first autologous ex vivo gene therapy approved by the EMA in 2016, 3 programs in advanced registrational studies in MLD (metachromatic leukodystrophy), WAS (Wiskott Aldrich syndrome) and ADA-SCID (adenosine deaminase severe combined immunodeficiency), 2 other clinical programs in X-CGD (X-linked chronic granulomatous disease) and beta-thalassemia, as well as an extensive preclinical pipeline.
- The company is partnered with world-leading institutions in gene therapy, including University College London, Great Ormond Street Hospital, the University of Manchester and Central Manchester University Hospitals, the University of California Los Angeles and Boston Children's Hospital, and Telethon Institute of Gene Therapy/Ospedale San Raffaele.
- Orchard is a publicly traded company (NASDAQ: ORTX) with offices in the UK and the US, including London, San Francisco and Boston.

Key people

- Mark Rothera, President, CEO
- Andrea Spezzi, Co-founder. Chief Medical Officer