BioPharmAnalyses

« *LANDSCAPE IN…* »

GENE THERAPY COMPANIES

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CONTENTS

CEVEC Pharmaceuticals

General Informations

Year founded : 2001
Location : Gottfried-Hagen-Straße 62, 51105 Köln, Germany
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Website: http://cevec.com/
https://www.linkedin.com/company/cevec-pharmaceuticals-gmbh/

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Management :

Nicole Faust, PhD, CEO & CSO (faust@cevec.com, https://de.linkedin.com/in/nicole-faust-7b49104)
Nico Scheer, PhD, Chief Business Officer (scheer@cevec.com, bizdev@cevec.com, https://fr.linkedin.com/in/nico-scheer-8397517a)
Hartmut, Tintrup, PhD, VP Business Development for Gene Therapy and Viruses (tintrup@cevec.com, https://www.linkedin.com/in/hartmut-tintrup-40aa046/)

Core Business in Gene Therapy: CDMO for Cell and Gene Therapy Products

Corporate Informations

Cevec Pharmaceuticals GmbH manufactures biopharmaceutical molecules with human glycosylation patterns. It provides therapeutic proteins and monoclonal antibodies. The company develops CAP-GO platform, which include Construction of optimized expression vectors, Serum- and animal component-free cell line generation, and Stable pool generation and single cell cloning for recombinant protein. It also offers CAP-GT platform, which industrial scale production of Lentiviral, Adenoviral, and AAV gene therapy vectors. Further, the company offers contract manufacturing services. CEVEC Pharmaceuticals GmbH has a strategic collaboration with BioLamina AB.

Recent Fundings

-Total funding amount : 21.04M€

-JUL 2015 : 4.5M€ (venture round)
-JUL 2011 : 6M€ (venture round)
-FEB 2010 : 5.4M€ (series B)
-NOV 2009 : 4M€ (series A)

-Main investors include : Investtodate (DE), Midas Capital (USA), Peppermint Venture Partners (DE).

Technology

CAP-Go enables the production of proteins previously out of reach representing a significant proportion of the human proteome that is notoriously difficult to express in conventional cell lines such as CHO. The CAP-Go expression platform comprises a portfolio of glyco-optimized human suspension cell lines for the highly efficient production of a broad range of difficult to express recombinant proteins with authentic human post-translational modifications or on demand tailor made glycosylation patterns.

CAP-GT is a fully scalable manufacturing platform for viral vector production. CEVEC has successfully developed CAP-GT suspension cell-derived viral packaging cell lines which enable better scale-up and competitive production costs when compared to adherent cell culture systems. CAP-GT suspension cell lines grow to high cell densities and show excellent productivity for a broad range of viruses. Gene therapy vectors such as lentivirus (LV), adenovirus (AV) and adeno-associated virus (AAV) can be produced at industrial scale.)

Latest Developments

Date	Subject / Title	Partner	Comments / Link
MAY 2018	CEVEC and CSL Limited sign exclusive license agreement for production of recombinant C1 Esterase Inhibitor using CEVEC's proprietary CAP®Go technology	CSL Ltd (AU)	Press Release
JAN 2018	CEVEC and CellGenix cooperation leads to expansion of CellGenix cytokine portfolio with CAP®Go technology-derived TGF-Beta1 for *ex vivo* cell culture	CellGenix (DE)	Press Release
JAN 2018	CEVEC to introduce new helper-free AAV packaging cell line for scalable stable gene therapy vector production at the Phacilitate Cell & Gene Therapy World Conference		Press Release
MAY 2017	CEVEC and PlasmidFactory announce collaboration regarding adeno-associated virus (AAV) production	Plasmid Factory (DE)	Press Release

Latest Related Publications / Results

Reference	Authors, Location	Results / Comments	Link
Biotechnol Bioeng. 2018 Apr 17	Weis BL et al. University of Applied Sciences Biberach, Biberach, Germany	Stable miRNA overexpression in human CAP cells: Engineering alternative production systems for advanced manufacturing of biologics using miR-136 and miR-3074	Abstract
J Biotechnol. 2017 Dec 10;263:11-20.	Gutiérrez-Granados S et al. Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Barcelona, Spain	This novel strategy significantly simplifies large-scale transient transfection, while suitable cell growth, transfection efficiency, and high quality VLP production are achieved	Abstract
Appl Microbiol Biotechnol. 2016 May;100(9):3935-47	Gutiérrez-Granados S et al. Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Barcelona, Spain	Optimized production of HIV-1 virus-like particles by transient transfection in CAP-T cells	Abstract

Fortress Biotech (Formerly known as Coronado Biosciences, Inc)

General Informations

NASDAQ : FBIO

Year founded : 2006
Location : 2 Gansevoort Street, 9th Floor, New York, NY 10014, USA
Phone: +1 781-652-4500
Website: http://www.fortressbiotech.com/
https://www.linkedin.com/company/fortress-biotech

FTE: 70
Management :

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Samuel Berry, Corporate Counsel (bsamuel@fortressbiotech.com, https://www.linkedin.com/in/samuel-berry-27201b11)
Nona Silver, VP Clinical Operations (https://www.linkedin.com/in/nova-silver-68728ba)
Arthur Ross, VP Business Development (rarthur@fortressbiotech.com, https://www.linkedin.com/in/arthur-ross-74ab5448)
Charles Buchen, Director Business Development (bcharles@fortressbiotech.com, https://www.linkedin.com/in/charles-buchen-md-24801266/)
Susan Sobolov, Director Program Management (ssusan@fortressbiotech.com, https://www.linkedin.com/in/susan-sobolov-3994848/)
Lee Rauch, Strategic Business Advisor (rlee@fortressbiotech.com, https://www.linkedin.com/in/leerauch)

Corporate Informations

Fortress Biotech, Inc. develops and commercializes pharmaceutical and biotechnology products. The company develops CNDO-109, a lysate that treats cancer-related and other conditions; tramadol HCl for managing postoperative pain; CAEL-101 for the treatment of amyloid light chain amyloidosis; and CEVA101 for severe traumatic brain injury in children and adults in the United States. It also develops CK-301 for treating patients with non-small cell lung cancer (NSCLC); CK-101 for the treatment of patients with epidermal growth factor receptor mutation-positive NSCLC; and antibodies that target glucocorticoid-induced TNFR-related protein and carbonic anhydrase IX, as well as anti-cancer agents that inhibit bromodomain and extra-terminal proteins, and poly polymerase. In addition, the company develops CUTX-101 for treating Menkes disease; preclinical adeno-associated virus gene therapies for treating mucopolysaccharidosis type 1, dysferlinopathies, and corneal transplant rejection; Triplex, which is in Phase II clinical study for preventing and treating cytomegalovirus (CMV); and Pentamer, a vaccine drug candidate for preventing CMV. Further, it offers Targadox®, a tablet for severe acne; Luxamend® wound cream; Ceracade® for treating dry skin conditions; Triderm® for treating eczema, dermatitis, allergies, and rash; and chimeric antigen receptor and engineered T cell therapies across various cancers. Additionally, it provides retail brokerage and wealth management services to high net worth individual and institutional clients; investment banking, merger and acquisition, and advisory services to micro, small, and mid-cap high growth companies; trades in securities; liquidity services; and tax preparation, fixed insurance sales, and licensed mortgage brokerage services.

Financial Highlights

-Market capitalisation : approx 186.75MUS$ (MAY 2018)

-As of MAR 2018

-Revenue : 55.4MUS$ (2017 : 44.7%MUS$)
-R&D : 25MUS$, of which $22.8 million was related to Fortress Companies (2017 : 7.1MUS$, of which $5.4 million was related to Fortress Companies)
-G&A : 13.5MUS$, of which $8.4 million was related to Fortress Companie (2017 : 10.3MUS$, of which $6.7 million was related to Fortress Companies)
-National Holdings' operating expenses : 50.8MUS$ (2017 : 43.1MUS$)

-As of DEC 31, 2017, Fortress' consolidated cas, cash equivalents, short term investments, cash deposits and restricted cash totaled 168.3MUS$ (172.6MUS$ as of SEP 30 2017, 105.2MUS$ as of DEC 31 2016)

-Net revenue as of DEC 31 2017 : 187.6MUS$ (16.5MUS$ as of DEC 31 2016)

-Total revenue as of DEC 31 2017 include 17.2MUS$ of Fortress revenue and 170.4MUS$ revenue form National Holdings Corp (« National »). Total revenue as of DEC 31 2016 includes 6.2MUS$ of Fortress revenue and 10.3MUS$ revenue from National.
-No revenue is attributable to National prior to Fortress' acquisition of the company in SEP 2016

Fortress Companies

In Gene Therapy

-Aevitas Therapeutics
-Cyprium Therapeutics
-Tamid Bio

Others

-Avenue Therapeutics (Management of moderate to moderately severe postoperative pain)

-Helocyte (Immunotherapies for the treatment or prevention of cancer and infectious diseases)

-Caleum Biosciences (AL Amyloidosis)

-Journey Medical Corp (Focused on developing, acquiring, licensing, and commercializing branded dermatology products)

-Cellvation (Cellular therapeutics for the treatment of traumatic brain injury)

-MustangBio (Development of novel immunotherapies based on chimeric antigen receptor – CAR- research)

-Checkpoint Therapeutics (Development and commercialization of novel, targeted non-chemotherapy, and immune-enhanced combination treatments for patients with solid tumor cancers)

Aevitas Therapeutics

Founded : AUG 2017

Corporate Informations

Aevitas Therapeutics, Inc is developing novel gene therapy approaches for complement-mediated diseases. The Company was formed based on technology that uses adeno-associated virus (AAV)-based gene therapy to restore lasting production of regulatory proteins, potentially providing a curative treatment for diseases with high unmet need. As regulators of the alternative pathway, irregularities in these proteins can play a vital role in numerous complement-mediated diseases, including atypical hemolytic uremic syndrome (aHUS) and paroxysmal nocturnal hemoglobinuria (PNH). Recent research has also suggested that complement regulatory proteins could play a key role in the pathogenesis of age-related macular degeneration. Aevitas is headquartered in New York City.

Pipeline

Indication	Product	Type / Mechanism of action	Discovery / Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Atypical hemolytic uremic syndrome, Paroxysmal nocturnal hemoglobinuria, AMD		AAV-based gene therapy	✓					

Cyprium Therapeutics

Founded : MAR 2017

Corporate Informations

Cyprium Therapeutics, Inc is focused on the development of novel therapies for the treatment of Menkes disease and related copper metabolism disorders. In March 2017, Cyprium entered into a Cooperative Research and Development Agreement (CRADA) with the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health (NIH), to advance the clinical development of Phase 3 candidate CUTX-101 (Copper Histidinate injection) for the treatment of Menkes disease. In addition, Cyprium and NICHD entered into a worldwide, exclusive license agreement to develop and commercialize adeno-associated virus (AAV)-based gene therapy, called AAV-ATP7A, to deliver working copies of the copper transporter that is defective in Menkes patients, and to be used in combination with CUTX-101.

Pipeline

Indication	Product	Type / Mechanism of action	Discovery /Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Menkes Disease (ODD FDA : MAY 2012)	CUTX-101	Copper Histidinate injection	✓	✓	✓	✓		

Menkes Disease (ODD FDA : JAN 2014)	AAV-ATP7A	AAV gene therapy	✓					

Tamid Bio

Launch : SEP 2017

Corporate Informations

Tamid Bio, Inc. (Tamid), a Fortress Biotech company, is dedicated to the development of adeno-associated virus (AAV) gene therapies in orphan diseases with unmet medical needs. Tamid has partnered with the University of North Carolina at Chapel Hill (UNC-Chapel Hill) and the UNC Gene Therapy Center in the development of Tamid-001, an AAV gene therapy that targets the ocular manifestations of Mucopolysaccharidosis type I (MPS I). This rare and progressively debilitating disorder is caused by the accumulation of glycosaminoglycans ("GAGs") in multiple organs. Tamid-001 will aim to provide sustained delivery of the missing enzyme, to remove the GAGs already in the eye and prevent future accumulation. Tamid has also in-licensed two earlier-stage assets from UNC-Chapel Hill which will target dysferlinopathies and corneal transplant rejection. Preclinical and early clinical research programs for these assets will be performed at the UNC Gene Therapy Center. Tamid is headquartered in New York City.

Pipeline

Indication	Product	Type / Mechanism of action	Discovery / Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Mucopolysaccharidosis type I (ocular manifestations)		AAV-based gene therapy	✓					

Latest Developments (Fortress Companies)

Date	Subject / Title	Fortress Company / Partner	Comments / Link
APR 2018	Checkpoint Therapeutics Reports Preclinical Data on BET Inhibitor CK-103 at the American Association for Cancer Research Annual Meeting	Checkpoint Therapeutics	Press Release
MAR 2018	Mustang Bio Reports Fourth Quarter and Full-Year 2017 Financial Results and Recent Corporate Highlights	Mustang Bio	Press Release
MAR 2018	Avenue Therapeutics Receives Notices of Allowance for Patent Applications Covering Methods of Administration for Intravenous Tramadol	Avenue Therapeutics	Press Release
MAR 2018	Caelum Biosciences Announces Updated Phase 1b Data Presented at 16th International Symposium on Amyloidosis	Caleum Biosciences	Press Release

MAR 2018	Checkpoint Therapeutics, Inc. Announces Pricing of Public Offering of Common Stock	Avenue Therapeutics	Press Release
FEB 2018	Fortress Biotech Announces Aevitas Therapeutics Enters Sponsored Research Agreement with the University of Massachusetts Medical School to Advance AAV Gene Therapies	Aevitas Therapeutics	Press Release
DEC 2017	Fortress Biotech Forms Subsidiary Tamid Bio to Develop Novel AAV Gene Therapies in Orphan Diseases With Unmet Medical Needs	Tamid Bio	Press Release
DEC 2017	Mustang Bio Announces License Agreement with Harvard University, and Research Collaboration with Beth Israel Deaconess Medical Center, to Develop CRISPR/Cas9-Enhanced CAR T Therapies	Mustang Bio	Press Release

NightstaRx Therapeutics

General Informations

NASDAQ: NITE

Year founded: 2013
Location : 215 Euston Road, London NW1 2BE, UK
Phone: +44 (0)20 7611 2077. enquiries@nightstartx.com
U.S. Office, 81 Hartwell Ave, Suite 100, Lexington, MA 02421, USA
Website: https://www.nightstartx.com/
https://www.linkedin.com/company/6355721/

FTE: 23
Management :

David Fellows, CEO (https://www.linkedin.com/in/dave-fellows-94876526/)
Tuyen Ong, M.D., EVP, Chief Development Officer (https://www.linkedin.com/in/tuyen-ong-6b5642b/)
Gregory Robinson, Ph.D., CSO (https://www.linkedin.com/in/gregory-robinson-88b6715/)
Senthil Sundaram, CFO (https://www.linkedin.com/in/senthil1/)
Aniz Girach, MBChB, CMO (https://www.linkedin.com/in/aniz-girach-16926717/)
Julian Hanak, SVP, Global Head of CMC (https://www.linkedin.com/in/julian-hanak-23b1474/)
Mark De Rosch, Ph.D., SVP, Regulatory Affairs and Quality Assurance (https://www.linkedin.com/in/mark-de-rosch-phd-fraps-26a8653/)

Core Business in Gene Therapy: AAV-based Gene Therapy for Rare Inherited Retinal Diseases

Corporate Informations

Nightstar Therapeutics is a clinical-stage company focused on developing and commercializing a pipeline of novel 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. Its 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. Nightstar Therapeutics is also developing NSR-RPGR for the treatment of X-linked retinitis pigmentosa (XLRP), an inherited X-linked recessive retinal disease characterized by mutations in the RPGR gene, leading to a lack of protein transport and a loss of photoreceptors. The company is also evaluating other in-licensing opportunities to broaden its pipeline.

Recent Fundings and Financial Highlights

-OCT 2017: 76.9MUS$ (IPO)
-JUN 2017 : 45.0MUS$ (series C)

-For the year ended December 31, 2017:

-Revenue: MUS$- (2016: MUS$-)

-R&D: 20.5MUS$ (2016: 10.2MUS$)
-G&A: 7.0 MUS$ (2016: 2.1MUS$)
-Net loss: 29.7MUS$ (2016: MUS$12.2MUS$)
-Cash, cash equivalents and marketable securities: 129.4MUS$ (2016 :10.1MUS$)

Pipeline

Four Products in Rare Inherited Retinal Diseases

Indication	Product	Type / Mechanism of action	Discovery / Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Choroideremia	NSR-REP1	Gene therapy. AAV vector serotype 2 containing the human REP1 gene	✓	✓	✓	Full enrolment expected by H1 2019		
X-linked retinitis pigmentosa	NSR-RPGR	Gene therapy. AAV vector serotype 8 containing the human RPGR gene	✓	✓	Initial data expected towards the end of 2018			
Stargardt's disease	NSR-ABCA4	Gene therapy	✓					
Best disease or Best Vitelliform Macular Dystrophy	NSR-BEST1	Gene therapy	✓					

Orphan Drug Designations

Product	Indication	EMA	FDA
NSR-RPGR (adenovirus-associated viral vector serotype 8 containing the human RPGR gene)	X-linked retinitis pigmentosa	FEB 2018	
NSR-REP1 (adeno-associated viral vector serotype 2 containing the human REP1 gene)	choroideremia	JUL 2014	NOV 2014

Clinical Trials

Two Products in Choroideremia and X-linked Retinitis Pigmentosa

ID	Product	Status	Phase	Start / Completion Date	Planned enrollment	Results / Comments	Collaboration, nb of sites	Other ID	Last Update
NCT03507686	AAV2-REP1	recruiting	II	NOV 2017 MAR 2020	15	Indication: choroideremia	1 location	GEMINI	APR 2018

NCT03496012	AAV2-REP1	recruiting	III	DEC 2017 MAR 2020	140	Indication: choroideremia	15 location	STAR	APR 2018
NCT03116113	AAV-RPGR	recruiting	I-II	MAR 2017 FEB 2019	24	Indication: X-linked Retinitis Pigmentosa	2 locations	XIRIUS	APR 2018
NCT03359551		recruiting		JUN 2015 NOV 2017	300	Natural History of the Progression of Choroideremia	2 locations	NIGHT	DEC 2017
NI				NI	NI	Natural History of the Progression of X-linked Retinitis Pigmentosa	NI	XOLARIS	

Latest Developments related to Gene Therapies

Date	Subject / Title	Partner	Comments / Link
MAR 2018	Nightstar Therapeutics Announces Initiation of STAR Phase 3 Registrational Trial for NSR-REP1 in Choroideremia		Press Release
NOV 2017	Nightstar Expands Pipeline with Novel Gene Therapy for the Treatment of Stargardt Disease	Oxford University Innovation (UK)	Press Release
AUG 2017	Nightstar Appoints Tuyen Ong as Chief Development Officer		Dr. Ong joins Nightstar from PTC Therapeutics, where he most recently served as chief medical officer. Prior to PTC, Dr. Ong served as vice president of global clinical development and operations at Bausch and Lomb (subsequently acquired by Valeant Pharmaceuticals International). Press Release

Latest Related Publications / Results (see table in the full report version)

Reference	Authors, Location	Results / Comments	Link
Retina. 2017 Nov 16. doi: 10.1097/IAE.0000000000001957	Al-Qahtani AA et al. Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, USA.	Scleral pits in choroideremia: Implications for Retinal Gene Therapy.	Abstract
Am J Ophthalmol. 2017 Jul;179:110-117. doi: 10.1016/j.ajo.2017.05.002	Hariri AH et al. Doheny Image Reading Center, Doheny Eye Institute, Los Angeles, California, USA	Measurement and Reproducibility of Preserved Ellipsoid Zone Area and Preserved Retinal Pigment Epithelium Area in Eyes With Choroideremia.	Abstract

ProQR Therapeutics

General Informations

NASDAQ: PRQR

Year founded: 2012
Location: Zernikedreef 9, 2333 CK Leiden, The Netherlands
Phone: +31 88 166 7000. info@proqr.com
Website: http://www.proqr.com/
https://www.linkedin.com/company/proqr-therapeutics-bv/

FTE: 140
Management:

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René Beukema,CDO (rbeukema@proqr.com,
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Gerard Platenburg, PhD,CIO (gplatenburg@proqr.com)
David Rodman, EVP Research & Development (drodman@proqr.com,
https://www.linkedin.com/in/david-rodman-190a9a15/)

Core Business in Gene Therapy: RNA Therapeutics, Antisense Therapeutics

Corporate Informations

ProQR Therapeutics is a clinical stage company that discovers and develops RNA-based therapies (RNA antisense oligonucleotides, Axiomer® Editing Oligonucleotides) for rare genetic ophtalmological diseases, debilitating skin diseases and cystic fibrosis. Its pipeline includes therapeutic candidates targeting Leber's congenital amaurosis 10 (LCA10), Usher syndrome, Fuchs endothelial corneal dystrophy (FECD), Stargardt's disease and dystrophic epidermolysis bullosa (DEB). In 2017, one of ProQR's programs that focused on CNS disorders was spun out into a new company, Amylon Therapeutics (see page XXX). Amylon is developing therapeutics for a rare genetic brain disease. ProQR retains a majority ownership stake and remains involved through membership on the Boards.

Recent Fundings and Financial HIghlights

-Market capitalisation : approx 149.19MUS$ (MAY 2018)

-FEB 2018: up to 7.5MUS$ (funding)
-NOV 2017: 20MUS$ (public offering)

-For the first quarter of 2018:

-R&D: 7.7MUS$ (2017: 8.0MUS$)
-G&A: 2.7MUS$ (2017: 2.3MUS$)
-Net loss: 10.7MUS$ (2017: 10.5MUS$)
-Cash, cash equivalents and marketable securities: 38MUS$

-For the year ended December 31, 2017

-Enterprise value : 33.06MUS$ (2016 : 58.13MUS$)
-R&D: 31.2MUS$ (2016: 31.9MUS$)

-G&A: 10.8MUS$ (2016: 9.5MUS$)
-Net loss: 11.3MUS$ (2016:8.8MUS$)
-Cash, cash equivalents, and available-for-sale securities were 48.1MUS$ (2016 : 35.9MUS$)

Pipeline

Sixteen Products in CF, DEB, Fibrosis and Ophtalmological Diseases

Indication	Product	Type / Mechanism of action	Discovery Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Cystic fibrosis F508del	QR-110 (eluforsen)	antisense oligonucleotide targeting the F508delta mutation of CFTR	✓	✓	Subject to a partnership			
Cystic fibrosis G542X	QRX-036	antisense oligonucleotide targeting "Class 1" mutations	✓					
Cystic fibrosis W1282X	QRX-042	antisense oligonucleotide targeting "Class 1" mutations.	✓					
Cystic fibrosis R553X	QRX-052	antisense oligonucleotide targeting "Class 1" mutations.	✓					
Cystic fibrosis 621+1G>T	QRX-065	antisense oligonucleotide targeting "Class 1" mutations.	✓					
Cystic fibrosis 1717-1G>A	QRX-075	antisense oligonucleotide targeting "Class 1" mutations.	✓					
LCA10 due to the p.Cys998X mutation in the CEP290 gene	QR-110 (eluforsen)	Antifibrotics; Oligoribonucleotides	✓	✓	I-II – 6 month treatment data expected in 2018			
Usher syndrome 2A exon 13	QR-421a[1]	(2'-O-(2-methoxyethyl)-modified antisense	✓	Expected to advance				

		oligonucleotide targeting exon 13 in the USH2A gene)		towards the clinic in 2018				
Usher syndrome 2A PE40	QR-411	antisense oligonucleotide targeting the c.7595-2144A>G mutation in intron 40 of the USH2A gene	✓					
Stargardt's disease c.5461-10T>C	QRX-1011	antisense oligonucleotide modulating splicing of the mRNA for ABCA4 protein	✓					
Fuchs endothelial corneal dystrophy	QRX-504	single stranded RNA oligonucleotide targeting mutation in the TCF4 gene	✓					
Dystrophic Epidermolysis Bullosa, DEB exon 73	QR-313	antisense oligonucleotide targeting exon 73 in the COL7A1 gene	✓	Phase 1/2 WINGS trial expected to start in 2018				
Dystrophic Epidermolysis Bullosa DEB exon 80	QRX-323	antisense oligonucleotide targeting exon 80 in the COL7A1 gene	✓					
Dystrophic Epidermolysis Bullosa, DEB exon 3	QRX-333	antisense oligonucleotide targeting exon 3 in the COL7A1 gene	✓					
Partially owned projects								
Fibrosis	2 projects[2]	axiomer editing	✓					

		oligonucleotides (EONs)						
Amyloidosis of the Dutch type (HCHWA-D), or Katwijk's disease	AT-010[3]	RNA-based oligonucleotide that induces splicing modulation in the mature Amyloid Precursor Protein mRNA	✓					

[1] Partnered with Foundation Fighting Blindness
[2] Partnered with Galapagos
[3] Partnered with Amylon Therapeutics

Orphan Drug Designations

Product	Indication	EMA	FDA
antisense oligonucleotide targeting the F508delta mutation of CFTR - anti-sense oligonucleotide consisting of 2'0-Me RNA with a phosphorothioate backbone	Cystic fibrosis	OCT 2013	SEP 2013
QR-110 (antisense oligonucleotide complementary to the exonic splicer enhancer sequence at intron 26 of the centrosomal protein 290 pre-mRNA)	Leber's congenital amaurosis	APR 2016	MAY 2016
QR-313 (antisense oligonucleotide targeting exon 73 in the COL7A1 gene)	Dystrophic epidermolysis bullosa	OCT 2017	SEP 2017
QR-411 (antisense oligonucleotide targeting the c.7595-2144A>G mutation in intron 40 of the USH2A gene)	Retinitis pigmentosa	MAR 2017	JUN 2016
QR-421 (antisense oligonucleotide targeting exon 13 in the USH2A gene)	Retinitis pigmentosa	AUG 2017	JUL 2017
QR-421a (2'-O-(2-methoxyethyl)-modified antisense oligonucleotide targeting exon 13 in the USH2A gene)	Retinitis pigmentosa	FEB 2018	NOV 2017

Clinical Trials

One Product for Cystic Fibrosis and Leber's Congenital Amaurosis

ID	Product	Status	Phase	Start / Completion Date	Planned enrollment	Results / Comments	Collaboration, nb of sites	Other ID	Last Update
NCT03140969	QR-110	recruiting	I-II	OCT 2016 DEC 2018	12	Indication: Leber's congenital amaurosis due to the c.2991+1655A>G Mutation (p.Cys998X) in the CEP290 gene	3 locations		MAR 2018
NCT02532764	QR-110	active, not recruiting	I-II	JUN 2015 SEP 2017	64	Indication: homozygous ΔF508 cystic fibrosis	European Commission 27 locations		AUG 2018

Latest Developments related to Gene Therapies

Date	Subject / Title	Partner	Comments / Link
APR 2018	ProQR Provides Enrollment Update on QR-110 Clinical Trial and Highlights Ophthalmology Presentations at ARVO		Press Release
APR 2018	ProQR Appoints ADAR Expert Dr. Peter A. Beal to Scientific Advisory Board to Focus on Axiomer® RNA A-to-I Editing Technology		Press Release
JAN 2018	ProQR and Galapagos Announce Research Collaboration on Fibrosis Targets Using ProQR's Axiomer® technology	Galapagos (Belgium)	Press Release

Latest Related Publications / Results

Reference	Authors, Location	Results / Comments	Link
Am J Hum Genet. 2018 Apr 5;102(4):528-539. doi: 10.1016/j.ajhg.2018.02.010.	Zarouchlioti C et al. UCL Institute of Ophthalmology, London ECIV 9EL, UK.	Antisense Therapy for a Common Corneal Dystrophy Ameliorates TCF4 Repeat Expansion-Mediated Toxicity.	Abstract Full Text
Eur Respir J. 2018 Mar 29;51(3)	Dittrich AS et al. University of Heidelberg, Heidelberg, Germany	The results suggest that surface-bound NE activity may play an important role in the pathogenesis and serve as novel biomarker in CF lung disease	Abstract
Int J Mol Sci. 2018 Mar 7;19(3)	Duijkers L et al. Radboud University Medical Center, 6525 GA Nijmegen, The Netherlands	AONs seem to be a promising tool to treat *CEP290*-associated LCA, not only in homozygous but also in	Abstract

		compound heterozygous carriers of the c.2991+1655A>G variant	
Nucleic Acid Ther. 2017 Dec;27(6):309-322. doi: 10.1089/nat.2017.0691.	Capaldi D et al. Ionis Pharmaceuticals, Carlsbad, California.	Impurities in Oligonucleotide Drug Substances and Drug Products.	Abstract

Wave Life Sciences

General Informations

NASDAQ : WVE

Year founded : 2012
Location : 733 Concord Avenue, Cambridge, MA 02138 USA
Phone: +1 617-949-2900. Fax: + 1 s617-949-2901. info@wavelifesci.com
Website : https://www.wavelifesciences.com/

FTE: NI
Management :

Paul Bolno, MD, CEO (https://www.linkedin.com/in/paul-bolno-4506a19/)
Chandra Vargeese, PhD, SVP Research and Drug Discovery (https://www.linkedin.com/in/chandra-vargeese-129237a/)
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Core Business in Gene Therapy: Oligonucleotides (Antisense, Exon Skipping, RNAi, Splicing…) for the Treatment of Genetic Diseases within the Central Nervous System and the Neuromuscular System

Corporate informations

Wave Life Sciences is a genetic medicines company focused on delivering therapies for patients with serious, rare and neurological disorders (i.e. genetic diseases within the central nervous system and the neuromuscular system). The company has developed a proprietary synthetic chemistry drug development platform that is used to design oligonucleotides candidates. These oligonucleotides target genetic defects to either reduce the expression of disease-promoting proteins or transform the production of dysfunctional mutant proteins into the production of functional proteins. Wave Life Sciences is also designing therapies that use any of the major molecular mechanisms employed by nucleic acid therapeutics, including antisense, ribonucleic acid interference (RNAi), splicing, and exon skipping. The company expects to initiate six development programs by the end of 2018. These programs include its three most advanced programs, which are in Huntington's disease, and Duchenne Muscular Dystrophy, and three additional development candidates. Wave Life Science is also evaluating oligonucleotides targeting MALAT1 for the treatment of genetic ophthalmologic diseases.
The company is collaborating with Pfizer to advance genetically defined targets for the treatment of metabolic hepatic diseases, such as nonalcoholic steatohepatitis. Pfizer may select up to five targets from discovery through the selection of clinical candidates. Two targets were declared upon initiation of the agreement, including Apolipoprotein C-III.
Wave Life Sciences is incorporated in Singapore. The company has four wholly-owned subsidiaries: Wave Life Sciences USA, a Delaware corporation; Wave Life Sciences Japan, a company organized under the laws of Japan (formerly Chiralgen); Wave Life Sciences Ireland, a company organized under the laws of Ireland, and Wave UK. Therapeutic development research and development activities are conducted in the company USA's facilities. Process development research and development activities are conducted in its Japan's facilities.

Financial Highlights

-As of MAR 2018:

-R&D: 29.2MUS$ (2017: 14.7MUS$)
-G&A: 8.0MUS$ (2017: 5.9MUS$)
-Net Loss: 35.2MUS$ (2017: 21.1MUS$)
-Cash and cash equivalents: 110.5MUS$

-For the year ended December 2017

-Revenues: 3.70MUS$ (2016: 1.48MUS$)
-R&D: 79.30MUS$ (2016: 40.81MUS$)
-G&A: 26.97MUS$ (2016: 15.99MUS$)
-Net Loss: 102.03US$ (2016: 55.40MUS$)
-Cash and cash equivalents: 142.50MUS$ (2016: 150.29MUS$)

-Main investors include : RA Capital Management (USA), Redmile Group (USA), Price T Rowe Associates (USA), FMR (USA), BlackRock (USA).

Pipeline

Six Programs in Amyotrophic Lateral Sclerosis, Duchenne Muscular Dystrophy, Frontotemporal Dementia and Huntington's Disease

Indication	Product	Type / Mechanism of action	Discovery/ Preclinical	Development Phases				Approved / Marketed
				Phase I	Phase II	Phase III	Phase IV	
Huntington's disease	WVE-120101	antisense oligonucleotide targeting disease-associated single nucleotide polymorphism (SNP), within the huntingtin gene: rs362307 (HTT SNP-1)	✓	✓	Ib/IIa			
Huntington's disease	WVE-120102	antisense oligonucletoide targeting disease-associated single nucleotide polymorphism (SNP), within the huntingtin gene: rs362331 (HTT SNP-2)	✓	✓	Ib/IIa			
Duchenne Muscular Dystrophy 51	WVE-210201	exon 51 skipping	✓	✓				
Duchenne Muscular Dystrophy 53	NI	exon 53 skipping	✓	Q1 2019				
Frontotemporal dementia (C9orf72)	WVE-3972-01	Antisense silencing the repeat containing transcript in C9orf72 gene	✓	Q4 2018				
Amyotrophic lateral sclerosis (C9orf72)	WVE-3972-01	Antisense silencing the repeat containing	✓	Q4 2018				

		transcript in C9orf72 gene						
Spinocerebellar ataxia 3	NI	Identification of a candidte targeting the ATXN3 gene by the end of 2018	✓					

Orphan Drug Designations

Product	Indication	EMA	FDA
antisense oligonucleotide targeting the U isoform of SNP rs362307	Huntington's disease		JUN 2016

Clinical Trials

Three Products in Huntington's Disease and Duchenne Muscular Dystrophy

ID	Product	Status	Phase	Start / Completion Date	Planned enrollment	Results / Comments	Collaboration, number of sites	Other ID	Last Update
NCT03225846	WVE-120102	recruiting	Ib/IIa	JUL 2017 SEP 2019	48	Indication: Huntington's disease Top-line data expected in H1 2019	2 locations	PRECISION-HD2	MAR 2018
NCT03225833	WVE-120101	recruiting	Ib/IIa	JUL 2017 SEP 2019	48	Indication: Huntington's disease Top-line data expected in H1 2019	2 locations	PRECISION-HD1	MAR 2018
NCT03508947	WVE-210201	recruiting	I	JAN 2018 SEP 2018	40	Indication: Duchenne Muscular Dystrophy Safety data anticipated in Q3 2018.	6 locations	WVE-DMDX51-001	APR 2018

Latest Developments related to Gene Therapies

Date	Subject / Title	Partner	Comments / Link
MAY 2018	Wave Life Sciences Highlights Progress on Hepatic Collaboration with Pfizer	Pfizer (USA)	Pfizer recently nominated the fourth and fifth final hepatic targets under the collaboration agreement between the two companies to develop genetically targeted therapies for the treatment of metabolic hepatic diseases, such as nonalcoholic steatohepatitis. Press Release
APR 2018	Wave Life Sciences and Deep Genomics Form Collaboration to Discover Novel Therapies for Genetic Neuromuscular Disorders	Deep Genomics (Canada)	The companies will analyze and test oligonucleotides against potential therapeutic targets within multiple genes implicated in neuromuscular disorders. The analysis will use Deep Genomics' machine learning platform to identify cause and effect relationships specific to neuromuscular-related targets that involve splicing regulation. Wave's propriety chemistry platform will be used to validate targets and elucidate the implications of target intervention across different phenotypes, with the goal of expanding Wave's pipeline of rationally designed oligonucleotides. Press Release
FEB 2018	Wave Life Sciences and Takeda Form Global Strategic Collaboration to Advance Therapies for Central Nervous System Disorders	Takeda (JP)	Under the collaboration, Wave will provide Takeda the option to co-develop and co-commercialize programs in Huntington's disease, amyotrophic lateral sclerosis, frontotemporal dementia and spinocerebellar ataxia type 3 . In addition, Takeda will have the right to license multiple preclinical programs targeting CNS disorders, including Alzheimer's disease and Parkinson's disease. Press Release
MAY 2016	WAVE Life Sciences Enters Collaboration with Pfizer to Develop Genetically Targeted Therapies for the Treatment of Metabolic Diseases	Pfizer (USA)	The collaboration is focused on the advancement of genetically defined targets for the treatment of metabolic diseases. Under the terms of the agreement, Pfizer will select, up to five targets.

			Three targets have been, including Apolipoprotein C-III. Press Release

Latest Related Publications / Results

Reference	Authors, Location	Results / Comments	Link
Nat Biotechnol. 2017 Sep;35(9):845-851..	Iwamoto et al. Wave Life Sciences, USA. Harvard University and Harvard Medical School USA.	The article describes the developmentof a scalable synthetic process that yields therapeutic antisense oligonucleotide having high stereochemical and chemical purity.	Abstract