

Amplifying gene expression with RNA-targeted therapeutics

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Supplementary TABLE 1 Gene therapy treatments approved by FDA or EMA**

Drug name	Company	Date	Transgene or target	Vector	Indication	Delivery Route	Status
Sipuleucel-T (Provenge®)	Dendreon Corp.	2010	PAP+GM-CSF	Autologous PBMC	Castrate resistant prostate cancer	IV infusion	
Alipogene tiparvovec (Glybera)	AMT/ UniQure	2012*	Lipoprotein lipase	AAV1	Lipoprotein lipase deficiency	Intramuscular injection	Discontinued in 2017 for cost
Talimogene laherparepvec (Imlygic / T-Vec / Oncovex)	BioVex/ Amgen	2015	Immunotherapy, tumor cell lysis	Herpes simplex virus 1	Melanoma	Injection into lesions	
Strimvelis	Orchard	2016*	Adenosine deaminase (ADA)	Autologous CD34+ stem cells / gamma-retrovirus	Adenosine deaminase-severe combined immunodeficiency	IV infusion	On hold due to mutagenesis concerns
Voretigene neparvovec (Luxturna)	Spark Ther., Children's Hospital of Philadelphia	2017	RPE65	AAV2 vector	Leber congenital amaurosis	Subretinal injection	
Axicabtagene ciloleucel (Yescarta)	Kite	2017	CD-19	CAR-T therapy, γ-retroviral vector	Diffuse large B-cell lymphoma; primary mediastinal large B-cell lymphoma	IV infusion	
Tisagenlecleucel (Kymriah)	Novartis	2017	CD-19	CAR-T therapy, lentiviral vector	B-cell acute lymphoblastic leukaemia, diffuse large B-cell lymphoma	IV infusion	
Onasemnogene APOB10 modulator (Zolgensma)	Novartis, AveXis	2019	SMN1	AAV9	Spinal muscular atrophy	IV infusion	
Betibeglogene autotemcel (Zynteglo)	Bluebird bio	2019	Beta-globin	Lentiglobin BB305, lentiviral vector	Beta thalassemia	IV infusion	
Atidarsagene autotemcel (Libmeldy)	Orchard	2020*	ARSA	Autologous CD34+ stem cells / lentivirus	Metachromatic leukodystrophy	IV infusion	
Brexucabtagene autoleucel (Tecartus)	Gilead/Kite	2020	CD-19	CAR-T therapy, replication-incompetent retroviral vector	Mantle cell lymphoma	IV infusion	
Elivaldogene autotemcel (Skysona)	bluebird bio	2021*	ALDP	Autologous CD34+ stem cells / lentiviral vector	Adrenoleukodystrophy	IV infusion	
Idecabtagene vicleucel (Abecma)	Celgene / BMS	2021	B-cell maturation antigen	CAR-T-cell therapy, lentiviral vector	Multiple myeloma	IV infusion	
Lisocabtagene maraleucel (Breyanzi)	Celgene / BMS	2021	CD-19	CAR-T therapy, replication-incompetent, self-inactivating lentiviral vector	Large B-cell lymphoma	IV infusion	
Lenadogene neparvovec (Lumevoq, GS010)	GenSight Biologics	2022*	ND4	Gene therapy, rAAV2/2-ND4	Leber's hereditary optic neuropathy	Intravitreal injection	
Etranacogene dezaparvovec (Hemgenix, CSL222 / AMT-061)	UniQure / CSL Behring		FIX	Gene therapy, AAV5	Hemophilia B	One-time IV infusion	
Ciltacabtagene autoleucel (Carvykti®)	Janssen Biotech	2022	Anti-BCMA	CAR-T cell therapy, replication incompetent lentiviral vector	Multiple myeloma	IV infusion	With cytokine release syndrome warning

Nadofaragene firadenovec-vncg (Adstiladrin®)	Ferring	2022	IFNα2b	Gene therapy, AAV5	Non-muscle invasive bladder cancer	Intravesical instillation	
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*Market authorization by EMA only

****Approved Cellular and Gene Therapy Products.** <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>

Supplementary TABLE 2 Nucleic acid-based therapeutics and RNA-targeting small molecules approved by FDA and EMA**

Drug name	Company	Date	Type	Target	Indication	Delivery Route
Fomivirsen (Vitravene)	Ionis, Novartis, Abbot	1998	RNAseH, PS ASO	UL123 gene of cytomegalovirus	Cytomegalovirus retinitis	Intravitreal injection
Pegaptanib (Macugen)	NeXstar, Gilead, OSI	2004	Aptamer, Pegylated PD, 2MOE, 2F ASO	VEGF antagonist	Age-related macular degeneration	Intravitreal injection
Mipomersen (Kynamro)	Ionis, Kastle	2013	RNAse H, PS 2MOE ASO	ApoB100	Homozygous familial hypercholesterolemia	SC
Ataluren (Translarna®)	PTC Therapeutics	2014*	Small molecule	Premature termination codon read-through	DMD	Oral
Eteplirsen (ExonDys51)	Sarepta	2016	Exon skipping, morpholino ASO	Dystrophin	Exon 51-related Duchenne muscular dystrophy	IV infusion
Nusinersen (Spinraza)	Ionis, Biogen	2016	Exon skipping, PS 2MOE ASO	SMN2	Spinal muscular atrophy	IT
Inotersen (Tegsedi)	Ionis, Akcea	2018	RNAse H, PS 2MOE ASO gapmer	TTR	Hereditary transthyretin-mediated amyloidosis	SC
Patisiran (Onpattro)	Alnylam	2018	siRNA in lipid nanoparticles	TTR	Hereditary transthyretin-mediated amyloidosis	IV
Golodirsen (Vyondys 53)	Sarepta	2019	Exon skipping, morpholino ASO	Dystrophin	Exon 53-related Duchenne muscular dystrophy	IV infusion
Milasen	Boston Children's Hospital	2019	Splice switching, PS 2MOE ASO	MFSD8	Batten disease	IT
Givosiran (Givlaari)	Alnylam	2019	siRNA, GalNAc-conjugated	ALAS1	Acute hepatic porphyria	SC
Viltolarsen (Viltepso)	Nippon Shinyaku Pharma	2020	Exon skipping, morpholino ASO	Dystrophin	Exon 53-related Duchenne muscular dystrophy	IV
Risdiplam (Evrysdi®)	Roche/PTC Therapeutics	2020	Splice-modulating small molecule	SMN2	Spinal muscular atrophy	Oral
Volanesorsen (Waylivra)	Ionis, Akcea	2020*	RNAse H, PS 2MOE ASO	ApoCIII	Familial chylomicronaemia	SC
Lumasiran (Oxlumo)	Alnylam	2020	RNAi, Enhanced Stabilization Chemistry-GalNAc	Glycolate oxidase (HAO1)	Primary hyperoxaluria type 1	SC
Casimersen (SRP-4045, AMONDYS 45)	Sarepta	2021	Exon skipping, PMO ASO	Dystrophin	Exon 45-related Duchenne muscular dystrophy	IV
Inclisiran (Leqvio)	Alnylam, The Medicines Company, Novartis	2020*, 2021	siRNA, Enhanced Stabilization Chemistry-GalNAc	PCSK9	Familial hypercholesterolemia	SC
Vutrisiran (Amvuttra™)	Alnylam	2022	siRNA-GalNAc	TTR	Hereditary transthyretin-mediated amyloidosis	SC

*Market authorization by EMA only

****Drugs@FDA: FDA-Approved Drugs.** <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>