Get Up to Speed with Gene Therapy: Pediatric Pharmacy Implications

Current and Upcoming Gene Therapies in the Pediatric Population

11/11/2025 | Celina Hung, PGY1 Pharmacy Resident, Advocate Christ Medical Center

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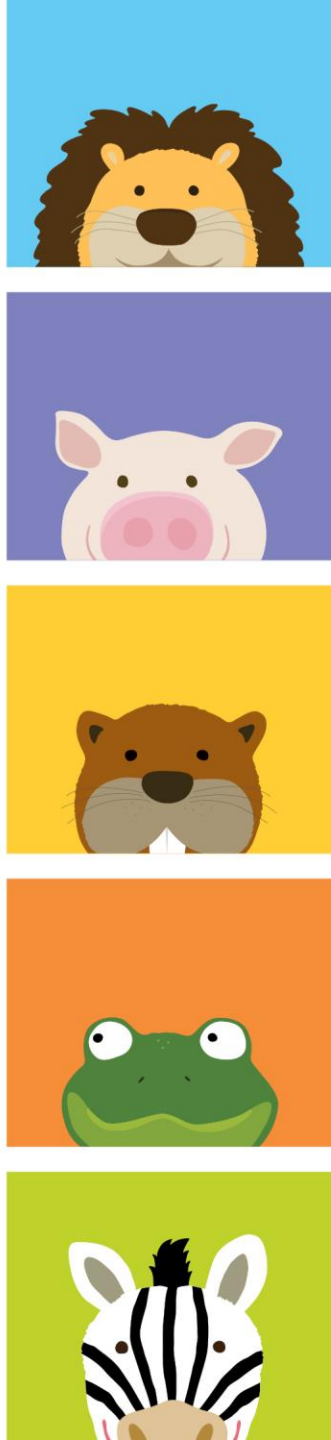
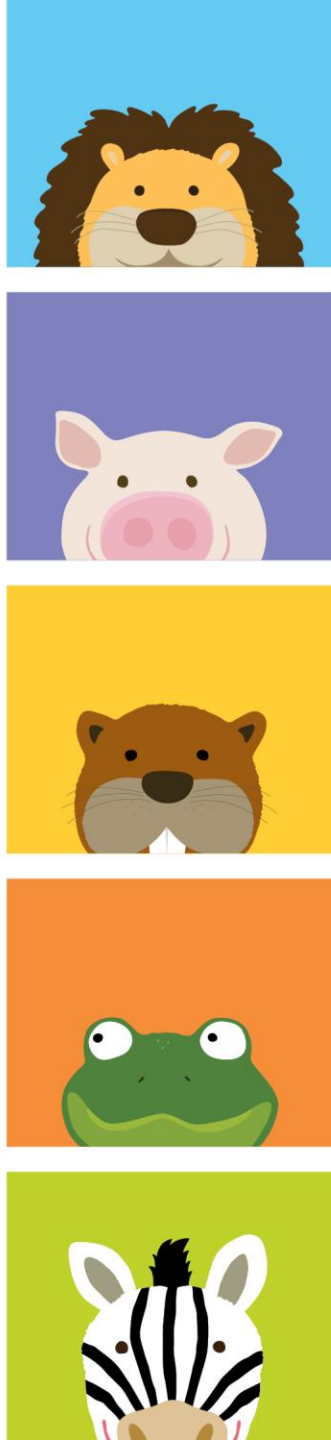
Disclosures

The planners and speakers have indicated that there are no relevant financial relationships with any ineligible companies to disclose.



Learning Objectives

- Recall the indications of FDA-approved pediatric gene therapies used within Advocate Health
- Recognize significant adverse reactions associated with gene therapies
- Identify the pharmacist's role in managing pediatric patients receiving gene therapy



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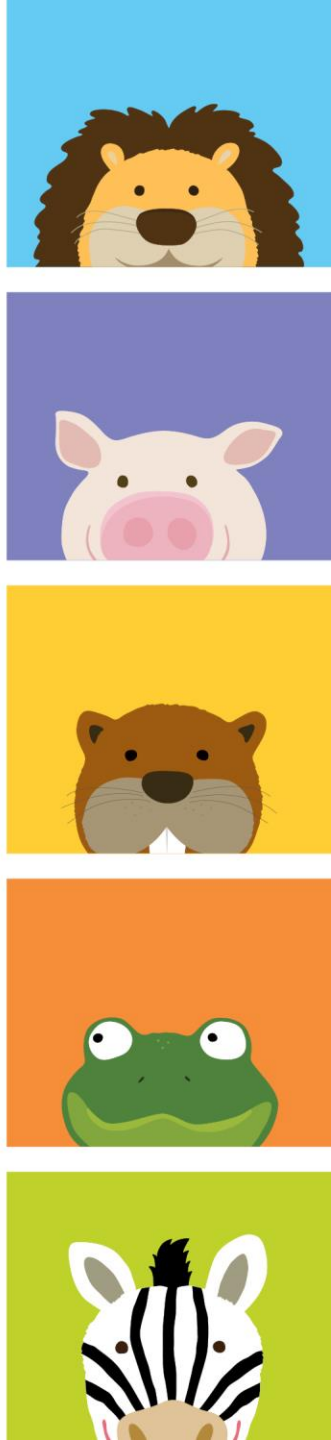
Abbreviations

- AADC: Aromatic l-amino acid decarboxylase
- AAVs: Adeno-associated viruses
- ABW: Actual body weight
- AdV: Adenoviruses
- AE: Adverse event
- BBW: Black box warning
- CRISPR: Clustered regularly interspaced short palindromic repeats
- CMAP: Compound muscle action potential
- DMD: Duchenne muscular dystrophy
- DNA: Deoxyribonucleic acid
- GVHD: Graft-versus-host disease
- HbF: Hemoglobin F
- HbS: Hemoglobin S
- HD: High-dose
- Hgb: Hemoglobin
- HSCT: Hematopoietic stem cell transplant
- HvGD: Host versus graft disease
- LNPs: Lipid nanoparticles
- LVs: Lentiviruses
- NSAID: Non-steroidal anti-inflammatory drug
- N/V: Nausea/vomiting
- RNA: Ribonucleic acid
- SAE: Serious adverse event
- SCD: Sickle cell disease
- SMA: Spinal muscular atrophy
- SMN1: Survival motor neuron 1
- TDT: Transfusion-dependent ß-thalassemia
- TEAE: Treatment emergent adverse event
- vg: Vector genomes
- WAC: Wholesaler acquisition cost
- WBC: White blood cell

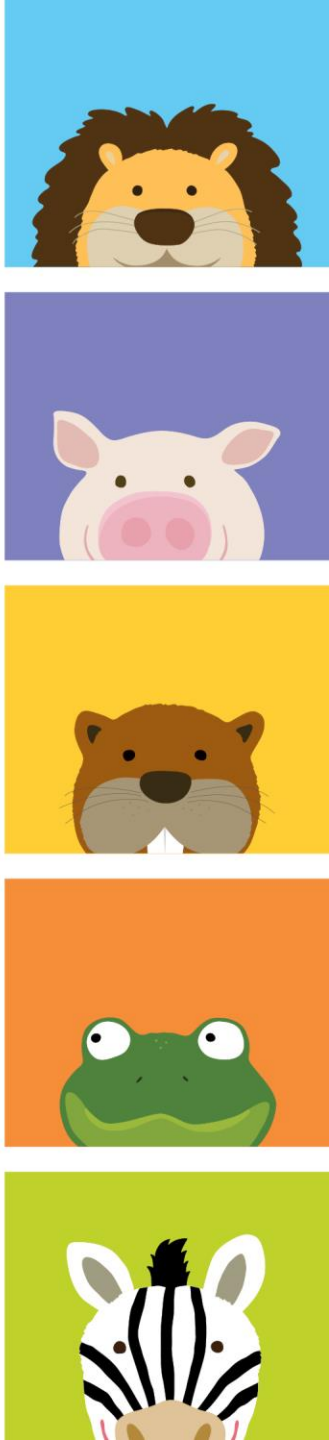


Background

What is Gene Therapy?

A medical approach which involves the modification of nucleic acids (i.e. DNA and RNA) to manipulate a patient's cell to promote treatment or prevention of disease

Can occur *in vivo* or *ex vivo*



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Kaufmann KB, et al. *EMBO Mol Med*. 2013;5(11):1642-1661.

Viral Vectors & Delivery Systems

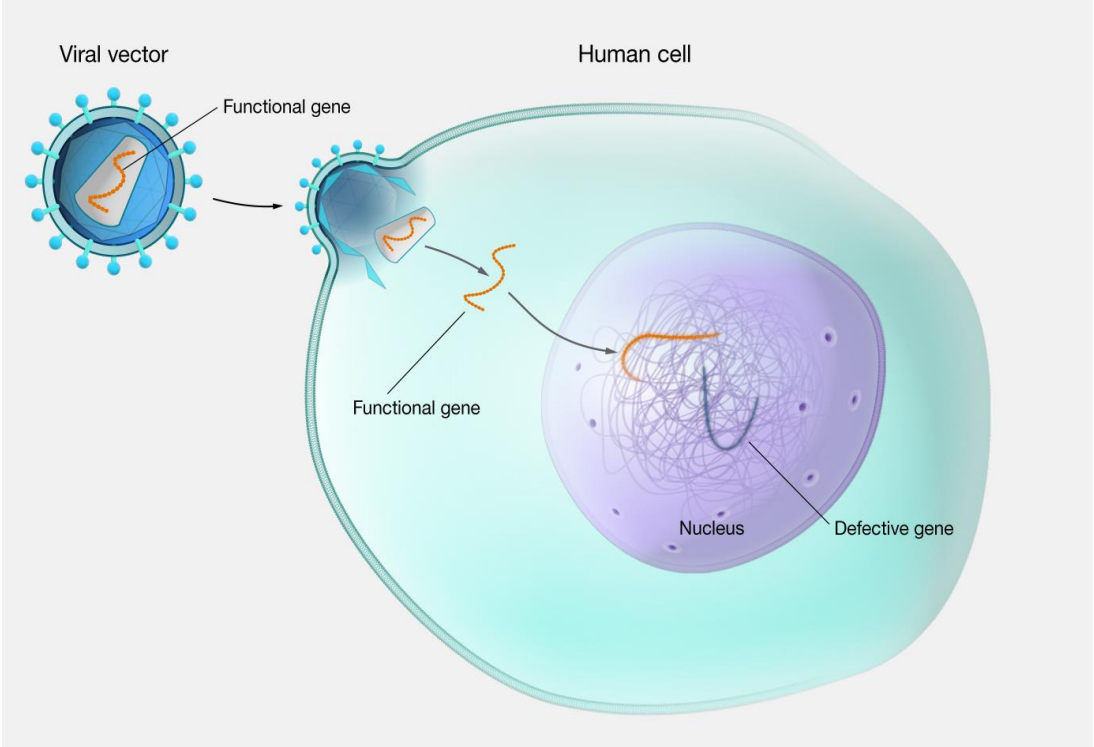
Most common delivery method for gene therapy

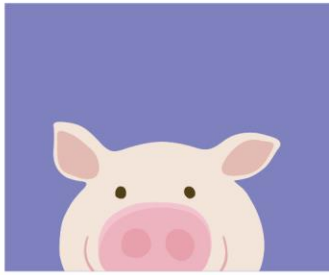
Key viral vector strategies:

- Adeno-associated viruses (AAV)
- Lentiviruses (LVs)

Nonviral delivery methods:

- Electroporation
- Lipid nanoparticles (LNPs)

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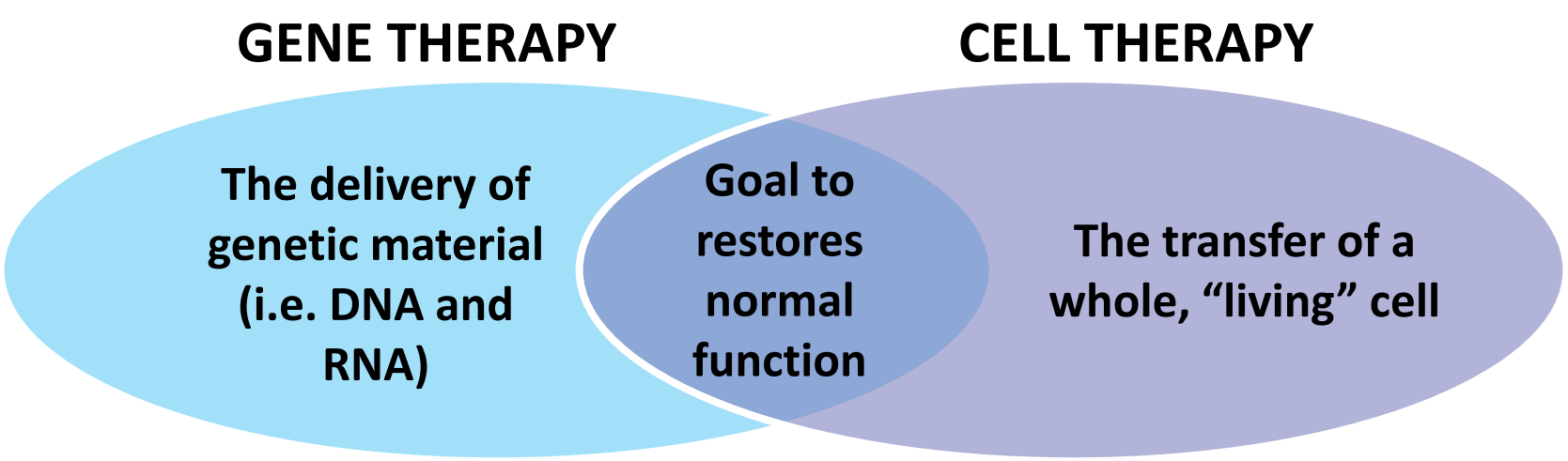
Chancellor D, et al. *Mol Ther.* 2023;31(12):3376-3388.

Gene Therapy vs Cell Therapy

- Cell Therapy: A medical approach that involves the transfer of intact, living cells to help treat or prevent disease



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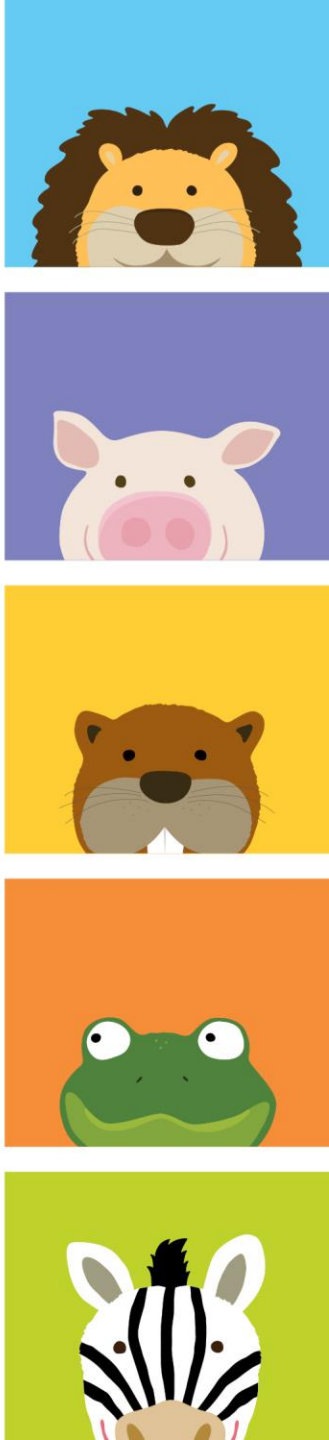


Chancellor D, et al. *Mol Ther*. 2023;31(12):3376-3388.

Autologous vs Allogeneic

Autologous

"customized"; utilizes the patient's own cells

Benefits:

- lower risk of GvHD

Limitations:

- $$$, availability, duration of manufacturing

Allogeneic

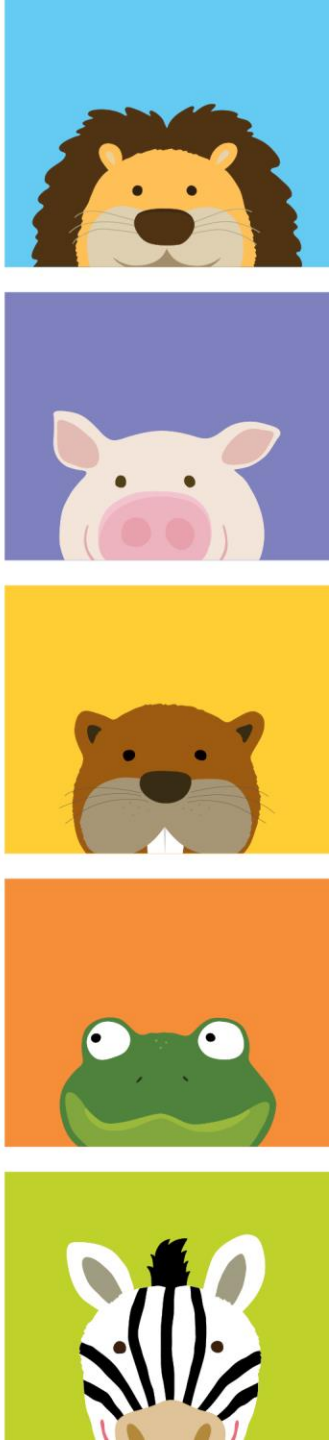
"off-the-shelf"; utilizes donor-derived cells

Benefits:

- $, standardized, quick availability

Limitations:

- higher risk of GvHD



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Emborg ME, et al. *Brain Research Bulletin*. 2025;224:111297

FDA Approved Gene Therapies in Pediatrics*

Exagamglogene autotemcel (CASGEVY)
- Sickle cell disease
- β-thalassemia

Delandistrogene moxeparvovec-rokl (ELEVIDYS)
- Duchenne muscular dystrophy

Eladocagene exuparvovec-tneq (KEBILIDI)
- Aromatic l-amino acid decarboxylase (AADC) deficiency

Tisagenlecleucel (KYMRIAH)
- Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

Atidarsagene autotemcel (LENMELDY)
- Pre-symptomatic late infantile (PSLI),
- pre-symptomatic early juvenile (PSEJ),
- OR early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD)

Voretigene neparvovec-rzyl (LUXTURNA)
- Confirmed biallelic RPE65 mutation-associated retinal dystrophy

Lovotibeglogene autotemcel (LYFGENIA)
- Sickle cell disease

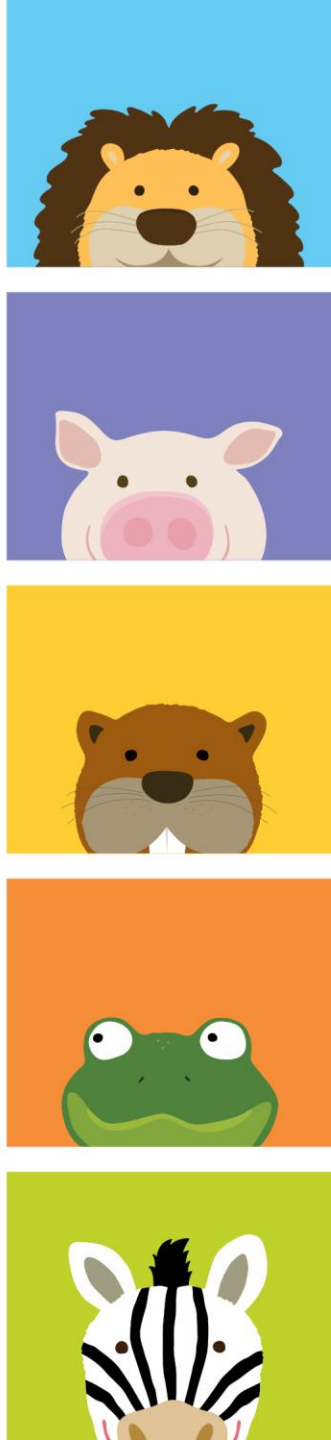
Elivaldogene autotemcel (SKYSONA)
- Active cerebral adrenoleukodystrophy (CALD)

Beremagene geperpavec-svdt (VYJUVEK)
- Dystrophic epidermolysis bullosa (DEB)

Prademagene zamikeracel (ZEVASKYN)
- Wounds with recessive dystrophic epidermolysis bullosa (RDEB)

Betibeglogene autotemcel (ZYNTEGLO)
- β-thalassemia

Onasemnogene abeparvovec-xioi (ZOLGENSMA)
- Spinal muscular atrophy



Black boarder = on formulary

*See *amendments* at end of slide deck

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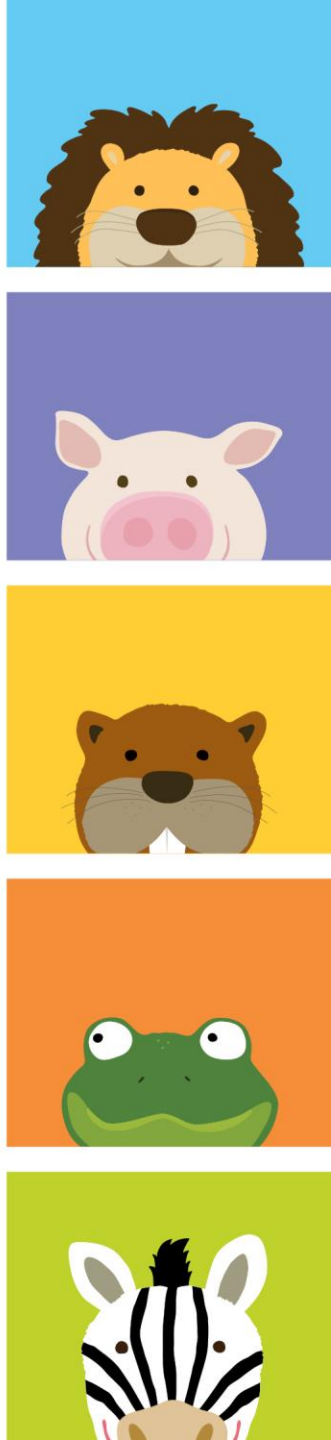
FDA. Approved Cellular and Gene Therapy Products. Updated August 15, 2025.

AH Available Gene Therapies for Pediatrics

DMD	• Delandistrogene moxeparvovec-rokl (*ELEVIDYS*)
SMA	• Onasemnogene abeparvovec-xioi (*ZOLGENSMA)*
*SCD	• Exagamglogene autotemcel (CASGEVY)

*Also indicated in TDT



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Duchenne Muscular Dystrophy

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What is DMD?

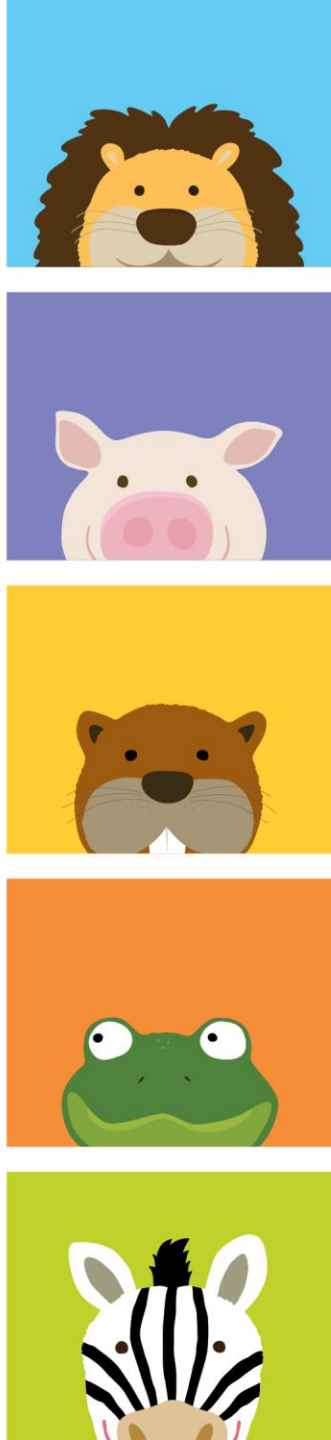
A severe, progressive, X-linked neuromuscular disorder seen amongst male pediatric patients that is caused by mutations of the *DMD* gene

Gene that encodes dystrophin protein; essential for motor function

- Mutations can lead to… ↓integrity of myofiber membrane, ↑muscle fiber degeneration

Affects 1 in 5000-6000 live male births

Average lifespan with optimal care: ~20-40 years old



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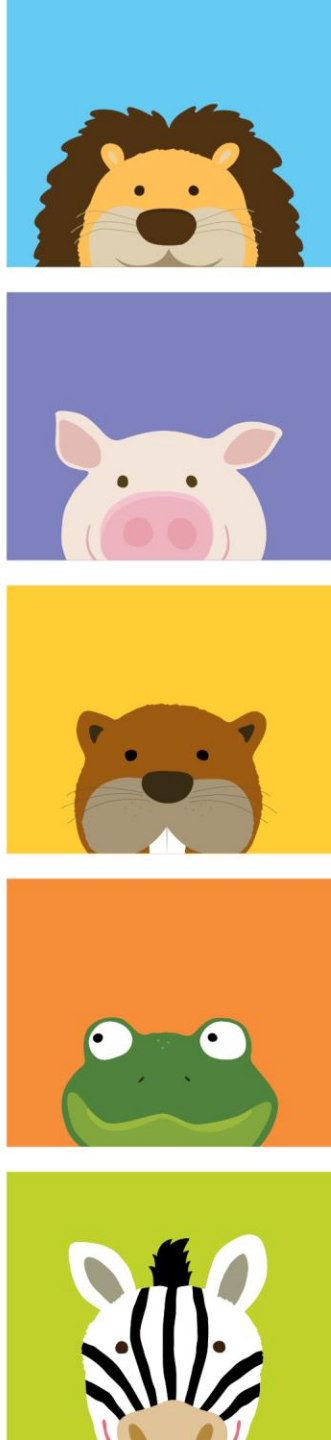
Venugopal V, et al. In: *StatPearls [Internet].* Jan 2025.

What is DMD?

- Progression of disease:

2-3 years old	10-12 years old	~20 years old
• Early signs of muscle weakness (e.g. frequent falls & difficulty climbing stairs)	• Wheelchair dependence	• Assisted ventilation



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Venugopal V, et al. In: *StatPearls [Internet]*. Jan 2025.

Current Management

Orthopedic Management

- Physical therapy

Pharmacological Management

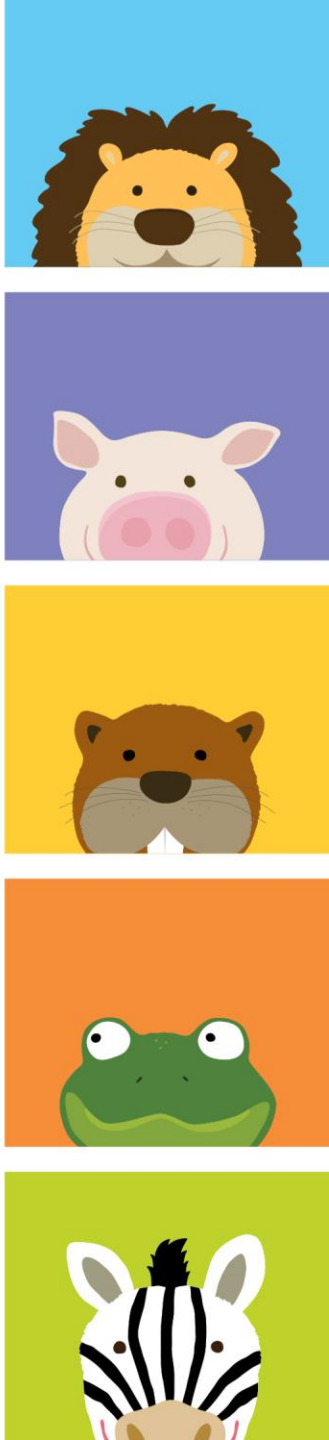
- Cardioprotective medications (e.g. ACEi, ARBs, BB)
- Corticosteroids (e.g. prednisone)

Respiratory Management

- Minimum annual respiratory function assessment
- Mechanical ventilation

Gene Therapy

- AH available gene therapy to consider: ***Delandistrogene moxeparvovec-rokl (Elevidys)***



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Angiotensin-converting enzyme inhibitors = ACEi
Angiotensin II receptor blockers = ARBs
Beta blockers = BB

Venugopal V, et al. In: *StatPearls [Internet]*. Jan 2025.

Delandistrogene moxeparvovec-rokl (ELEVIDYS)

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Delandistrogene moxeparvovec-rokl (ELEVIDYS)

An AAV vector-based gene therapy

Mechanism of Action:

- A non-replicating, recombinant AVV serotype rh74 capsid based gene therapy that delivers a micro-dystrophin transgene that distributes into target muscle tissue groups

Indications:

- Ambulatory patients with DMD who have a confirmed *DMD* gene mutation
- Non-ambulatory patients who have a confirmed *DMD* gene mutation → accelerated approval (currently on hold)
- Age requirement: ≥4 years old

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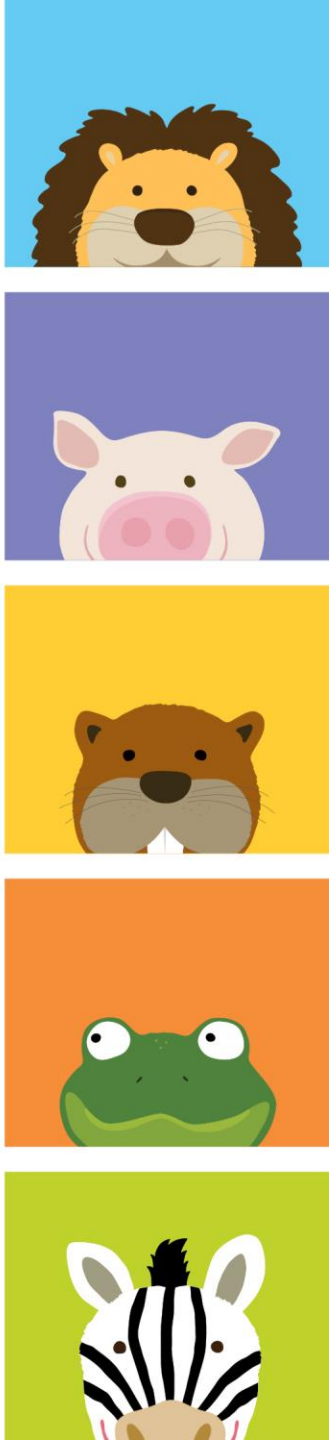
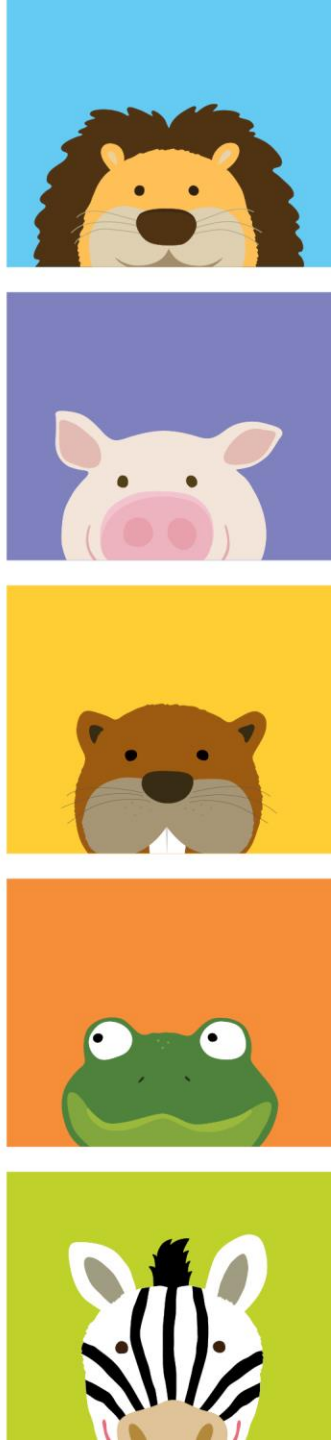


FDA. Elevidys [package insert]. *Sarepta Therapeutics, Inc.* Revised June 2024. Accessed September 13, 2025.

Delandistrogene moxeparvovec-rokl (ELEVIDYS)



Contraindications:

- Patients identified with deletion in exon 8 and/or exon 9 *DMD* genes

Additional Eligibility Considerations:

- Region of mutations
  - Limited data for deletions in exons 1-17 and/or 59-71
- Ineligible if pre-existing anti-AAVrh74 antibodies ≥1:400
- Patient baseline for liver function, platelet count, troponin-I levels

Warnings / Precautions:

- Can cause infusion-related reactions, acute serious liver injury, and myocarditis
- Risk of immune-mediated myositis due to deletions in the following regions: exons 1-17 and/or exons 59-71
- Vaccinations should be updated 4 weeks prior to the start of corticosteroid regimen
- Presence of infection symptoms → risk of serious complications

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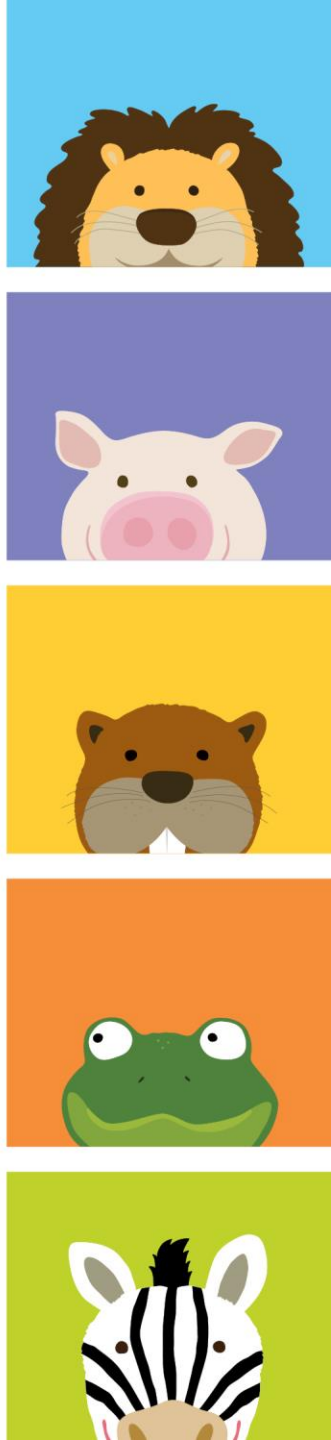
Delandistrogene moxeparvovec-rokl (ELEVIDYS)



Adverse Reactions:

- N/V, liver injury, thrombocytopenia, pyrexia

Toxicities:

- Hepatotoxicity

Monitoring Parameters:

- Signs and symptoms of hypersensitivity during or 3hrs post-infusion
- Signs and symptoms of myositis
- Liver function (e.g. liver enzymes, bilirubin) before and weekly x3 months post-infusion
- Platelet count before and weekly x2 weeks post-infusion
- Troponin-I before infusion and weekly x1 month post-infusion
- Vital signs prior, during, and post infusion (>10% of “normal”)

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FDA. Elevidys [package insert]. *Sarepta Therapeutics, Inc.* Revised June 2024. Accessed September 13, 2025.

Delandistrogene moxeparvovec-rokl (ELEVIDYS)

Dosing (in ABW):

- One time dose
- 10 to 70 kg: 1.33×10^{14} vg/kg
- 70 kg or greater: 9.31×10^{15} vg
- Dosing by mL:
  - Weight range dose rounding per table that contains 61 different rounded dose kit sizes

Weight range (kg)	Dose volume (mL)
41.5-42.4	420
42.5-43.4	430
43.5-44.4	440
44.5-45.4	450
45.5-46.4	460
46.5-47.4	470
47.5-48.4	480
≥69.5	700

Infusion Highlights:

- Dose is prepared using a split syringe functionality built in EPIC
- Infuse Elevidys via infusion pump over 1-2hrs via at a rate of <10 mL/kg/hour
- Flush line with normal saline before and after administration

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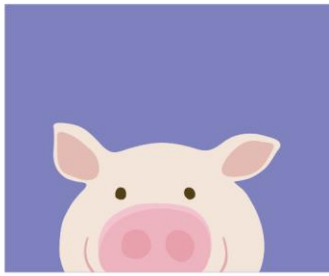


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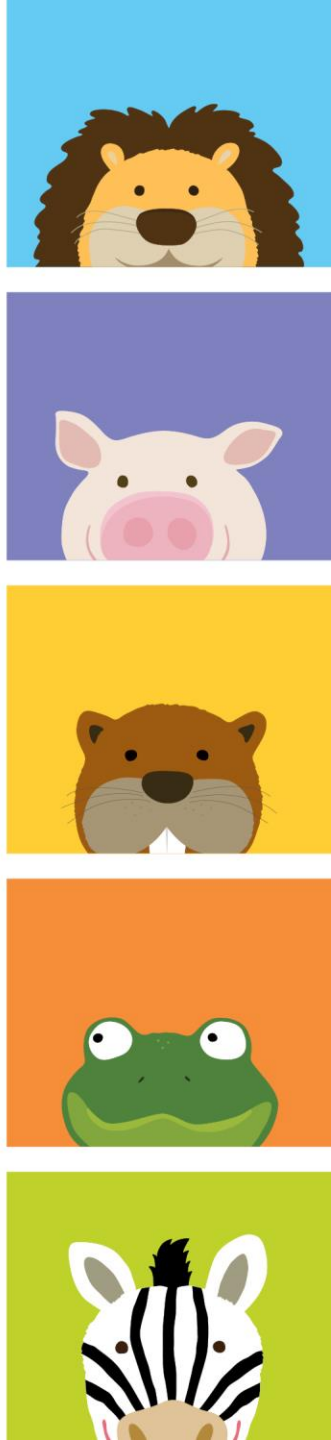
Delandistrogene moxeparvovec-rokl (ELEVIDYS)

- Concomitant Therapy:
  - Corticosteroid (i.e. prednisone or prednisolone) dosing requirements prior to infusion

Baseline corticosteroid	Dose volume (mL)
Daily/intermittent	**One day prior to infusion: initiate prednisone 1mg/kg/day + continue baseline dose**
HD x2days/wk	**One day prior to infusion: initiate prednisone 1mg/kg/day on days without HD corticosteroids + continue baseline dose**
No corticosteroids	**One week prior to infusion: initiate prednisone 1.5mg/kg/day**

  - Recommended maximum corticosteroid dose/day: prednisone 60mg



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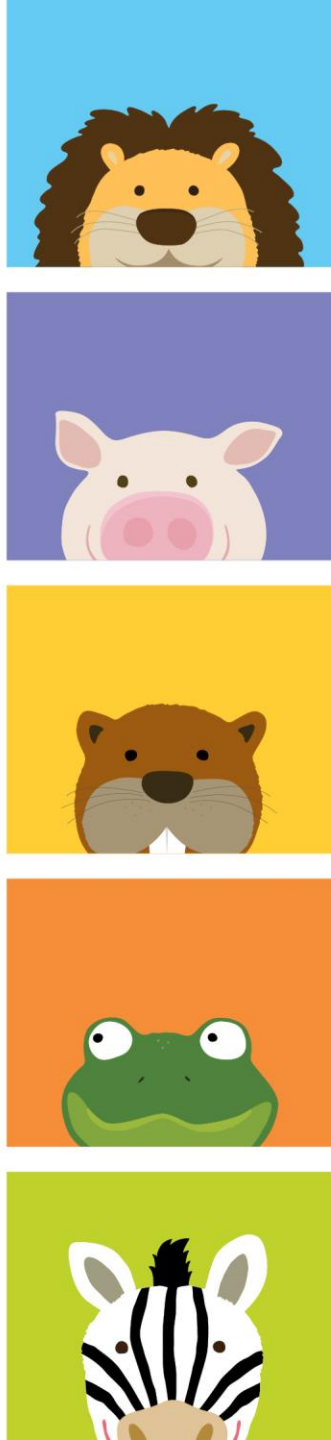
Delandistrogene moxeparvovec-rokl (ELEVIDYS)

- Post-infusion:
  - Corticosteroid (i.e. prednisone or prednisolone) dosing requirements post infusion for a minimum of 60 days for all patients

Baseline corticosteroid	Dose volume (mL)
Daily/intermittent	**Increase dose to prednisone 2mg/kg/day + continue baseline dose**
HD x2days/wk	**Increase dose to prednisone 2mg/kg/day on days without HD corticosteroids + continue baseline dose**
No corticosteroids	**Increase dose to prednisone 2.5mg/kg/day**

  - Recommended maximum corticosteroid dose/day: prednisone 120mg



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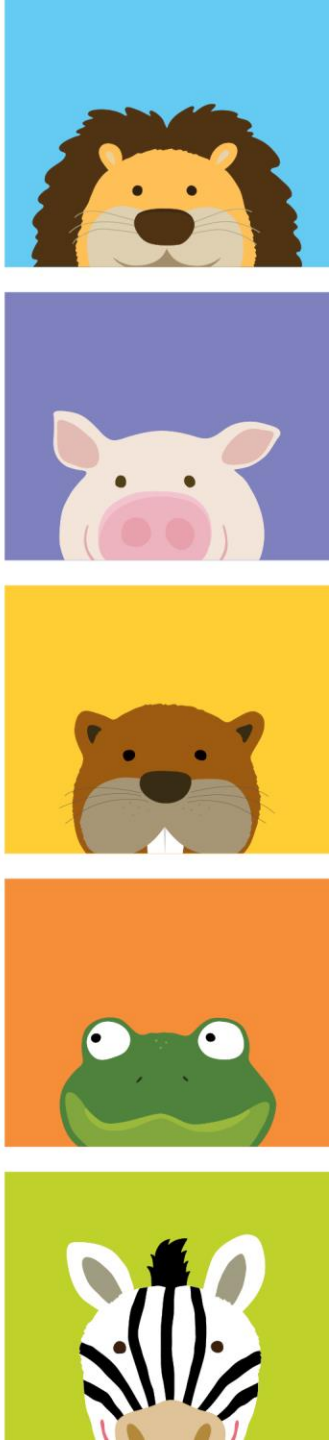

Available as a therapy plan under AH

Procurement / Use Criteria:

- ONLY by neuromuscular specialists in MDA clinics for DMD with qualifying mutations for outpatient use
- Involves “white bag” or “buy and bill” decision
- Requires agreement with payer prior to ordering

Storage & Handling:

- Shipped and delivered frozen (≤60°C) in 10mL vials; keep frozen
- May be refrigerated, upright for ≤14 days at 2-8°C; must be used once brought to room temperature; do not refreeze
- BUD in syringe or vials: 24hrs in room temperature
- Practice proper hygiene (e.g. hand washing) when in direct contact with gene therapy
- Place body fluids and waste in sealable bags x1 month post infusion

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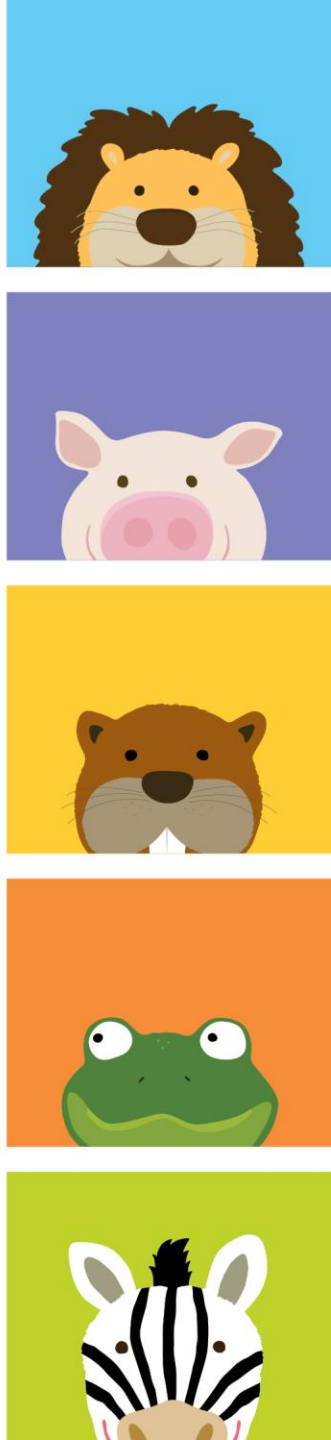
FDA. Elevidys [package insert]. *Sarepta Therapeutics, Inc.* Revised June 2024. Accessed September 13, 2025.

Delandistrogene moxeparvovec-rokl (ELEVIDYS)

- Cost considerations:

Elevidys
~$3.2 million (WAC)

Total Annual Cost of Illness
~$72,000 per year



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Landfeldt E, et al. *Neurology*. 2014;83(6):529-536

Delandistrogene moxeparvovec-rokl Literature Review

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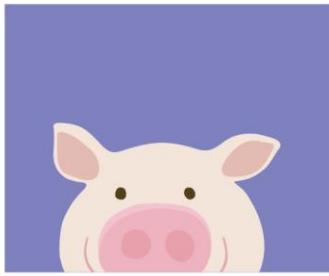
AAV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial



Purpose: Determine the safety and efficacy of delandistrogene moxeparvovec in pediatric patients with DMD

Inclusion Criteria

- Male pediatric ambulatory patients ages 4 to <8 years old at time of randomization
- Definitive DMD diagnosis per prior genetic testing/documented clinical findings
- Baseline oral corticosteroid dose/day ≥12 wks prior to screening
- Non-elevated rAAVrh74 antibody titers
- Mutation or premature stop codon between exons 18-79 EXCEPT exon 45

Intervention

- 1:1 randomization to receive a one-time dose of delandistrogene moxeparvov [1.33×10^{14} vector genomes per kilogram (vg/kg)] or matching placebo

Outcomes

- Primary:
  - Improvement in the NorthStar Ambulatory Assessment (NSAA) score from baseline to week 52
- Secondary:
  - Time to rise
  - 10-meter walk/run
  - Mean micro-dystrophin expression at week 12
  - Safety data

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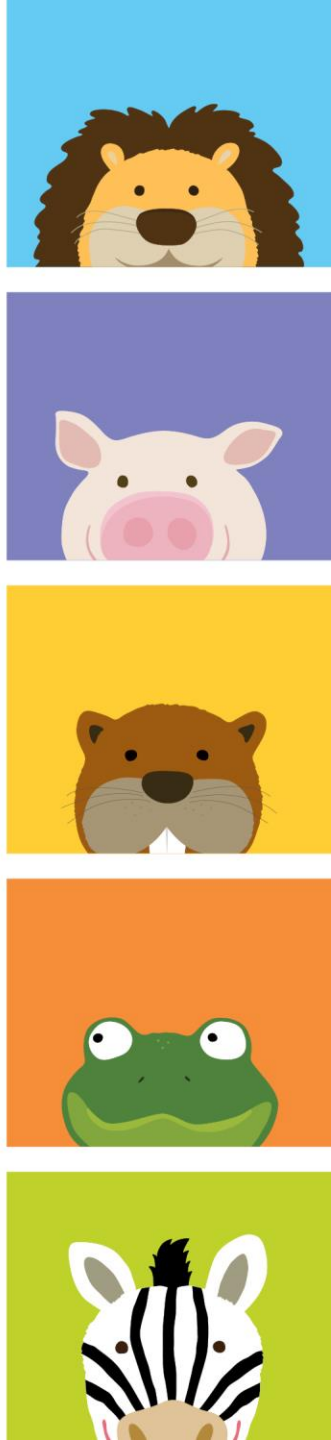
Mendell JR. *Nat Med*. 2025;31(1):332-341.

AV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial

		Delandistrogene moxeparvov (n = 63)	Placebo (n = 61)	LSM Difference (95% CI)	P-value
Primary Endpoint	***Total NSAA Score**	2.57	1.92	0.65 (-0.45, 1.74)	0.2441
Key Secondary Endpoints	***Average Time to Rise in Seconds**	-0.27	0.37	-0.64 (-1.06, -0.23)	-
	***Average 10-meter Walk/Run in Seconds**	-0.34	0.08	-0.42 (-0.71, -0.13)	-

*Change from baseline to week 52



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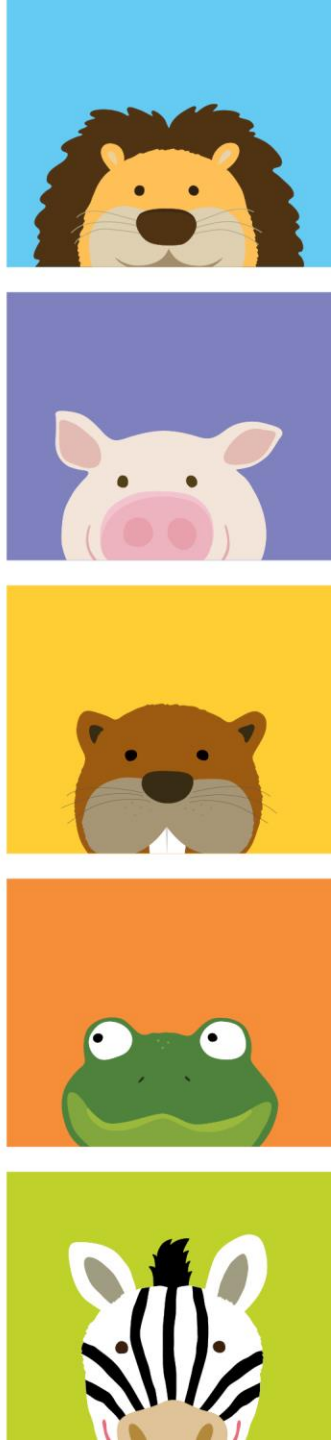
Mendell JR. *Nat Med*. 2025;31(1):332-341.

AV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial

		Delandistrogene moxeparvov (n = 17)	Placebo (n = 14)
Other Secondary Endpoint	**Micro-dystrophin expression at 12 weeks post-infusion n (%)**	34.29 (41.0)	0 (0)

*Subset of patients



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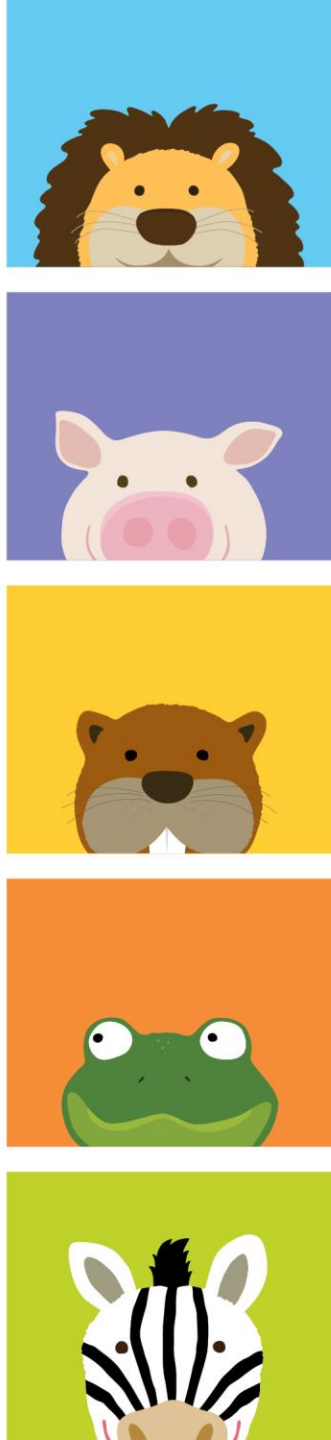
AV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial

Incidence of Adverse Events, n (%)		
	Delandistrogene moxeparvovec (n = 63)	Placebo (n = 61)
Patients with ≥1 AE	62 (98.4)	57 (91.9)
Patients with ≥1 SAE	14 (22.2)	5 (8.1)
Patients with ≥1 TEAE	62 (98.4)	57 (91.9)
Incidence of TR-TEAEs Occurring in >10% of Patients, n (%)		
Vomiting	62 (98.4)	57 (91.9)
Nausea	14 (22.2)	5 (8.1)
Decreased appetite	62 (98.4)	57 (91.9)



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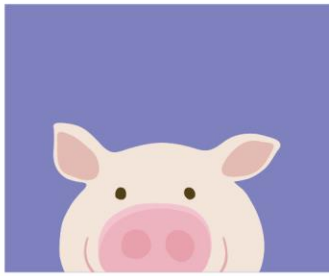
Mendell JR. *Nat Med*. 2025;31(1):332-341.

AV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial


Conclusion

- No statistical difference in the NSAA score from baseline to week 52 between the intervention and treatment group
- Intervention group was numerically favored amongst other endpoints (e.g. the average time to rise from the floor in seconds)
- Safety outcomes were in line with expectations and manageable in comparison to previous studies

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Mendell JR. *Nat Med*. 2025;31(1):332-341.

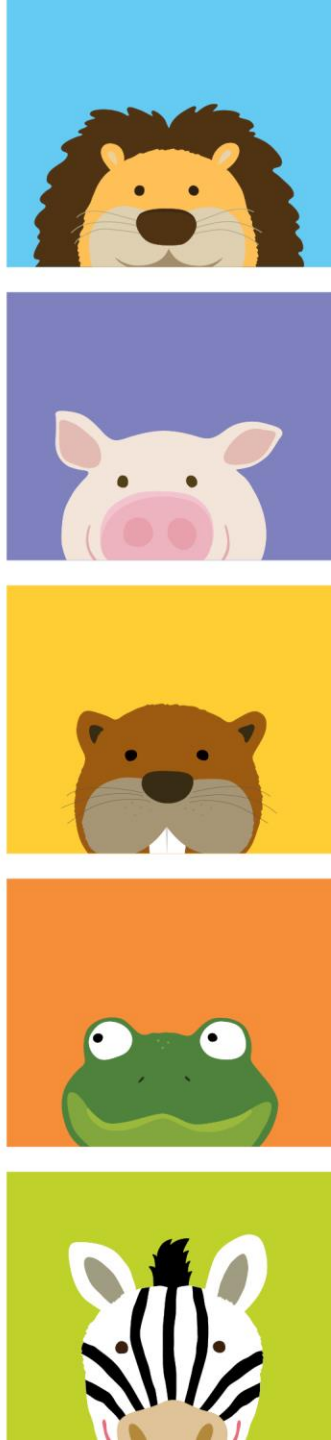
Recent Setbacks

July 18, 2025:

- FDA announced that a clinical trial involving Elevidys was to be put on hold due to safety concerns following 3 deaths
  - Concern of acute liver failure
- Ultimately paused shipments of Elevidys for review of safety information

July 28, 2025:

- FDA recommended to remove voluntary hold of Elevidys for ambulatory patients with DMD as the cause of the third death was not related to the product
  - The use and clinical trials of Elevidys for non-ambulatory patients remain on voluntary hold following two deaths related to acute liver failure with serious outcomes



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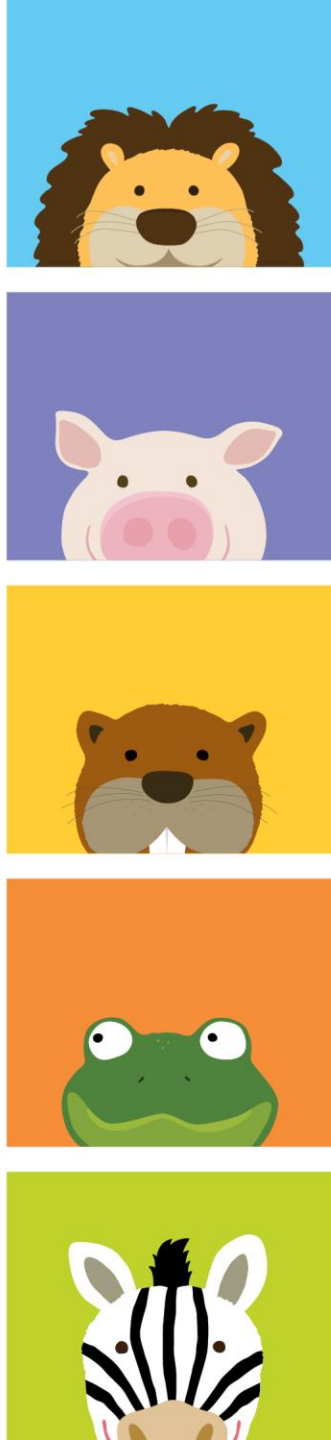
FDA. FDA Requests Sarepta Therapeutics Suspend Distribution of Elevidys and Places Clinical Trials on Hold for Multiple Gene Therapy Products Following 3 Deaths. July 18, 2025.
FDA. FDA Recommends Removal of Voluntary Hold for Elevidys for Ambulatory Patients. July 28, 2025.

Assessment Question #1

- Delandistrogene moxeparvovec-rokl (*Elevidys*) is indicated for children with Duchenne muscular dystrophy (DMD). Which of the following pediatric patients would be the most appropriate candidate for this gene therapy?
  - A) A non-ambulatory 2-YO boy with a confirmed *DMD* gene mutation
  - B) A non-ambulatory 7-YO boy with a confirmed *DMD* gene mutation
  - C) An ambulatory 4-YO boy with a confirmed *DMD* gene mutation involving exon 8
  - D) An ambulatory 6-YO boy with a confirmed *DMD* gene mutation and anti-AAVrh74 antibodies <1:400



Spinal Muscular Atrophy

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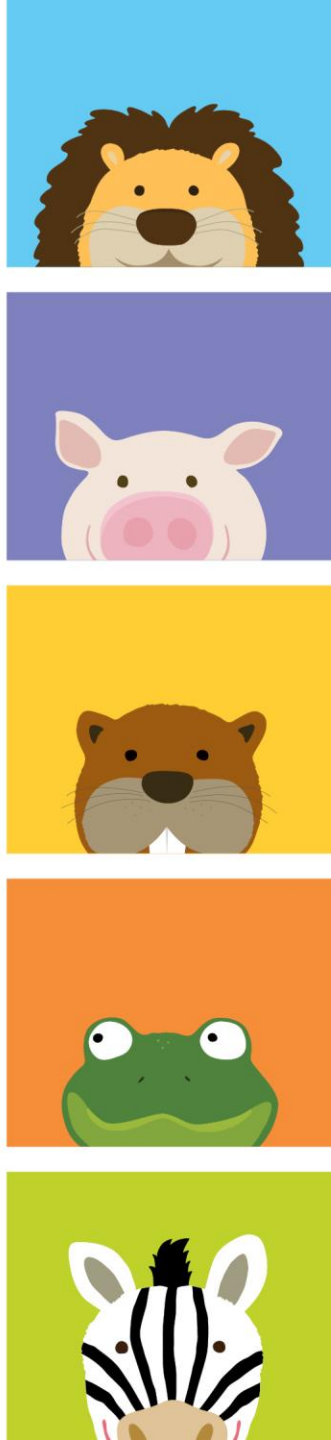
What is SMA?

A progressive, inherited autosomal recessive neurodegenerative disorder seen most often amongst pediatric patients with mutations of the *SMN1* gene on chromosome 5.

- Gene involved with survival of motor neurons

Affects 1 in 10,000 live male births

Average lifespan varies based on SMA type



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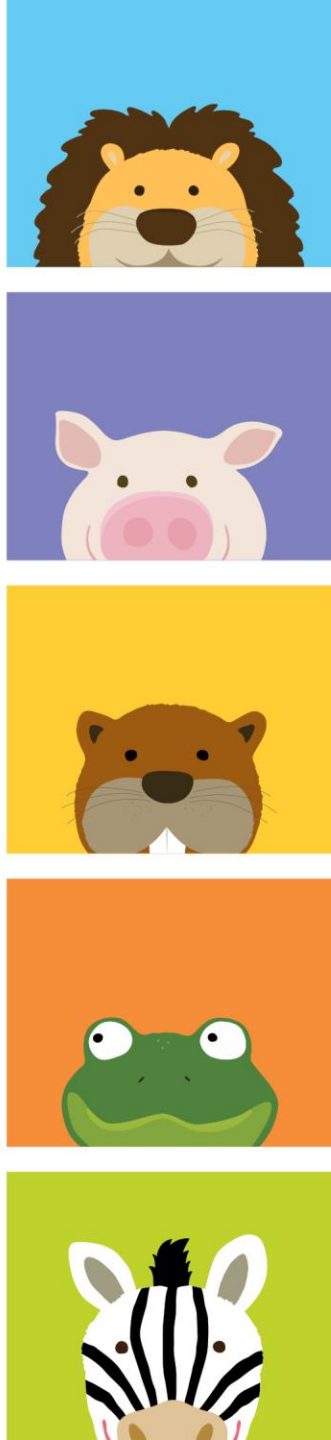
Burr P, et al. In: *StatPearls [Internet].* Jan 2025.
Mercuri, E, et al. *Nat Rev Dis Primers* 8, 52 (2022)

Progression of SMA

Type of SMA	Age of Onset	Function limitations	Life Expectancy
Type 0	Fetal	Weakness, decreased fetal movements, early respiratory failure	Days-weeks
Type I	0-6 months	Unable to sit or roll, requires feeding, communication, and pulmonary support	Months (median ~10mo)
Type II	7-18 months	Unable to walk, often needs pulmonary support	Years (median >20 years)
Type III	1.5-10 years	Limited walking capabilities, potential reduction in pulmonary function	Normal
Type IV	>18 years	None	Normal



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Mercuri, E. *Nat Rev Dis Primers* **8**, 52 (2022)

Current Management*

Orthopedic Management

- Physical therapy

Gastrointestinal Management

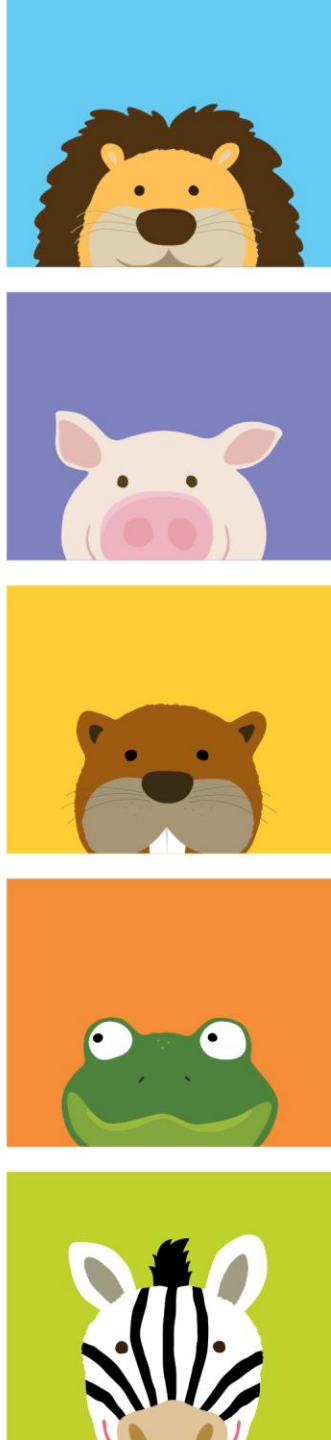
- Laparoscopic gastrostomy and Nissen fundoplication
- Assessment of nutritional status

Respiratory Management

- Regular respiratory function assessments
- Mechanical non-invasive ventilation
- Assisted cough techniques

Gene Therapy

- AH available gene therapy to consider: *Onasemnogene abeparvovec-xioi*



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Burr P, et al. In: *StatPearls [Internet]*. Jan 2025.
Mercuri, E. *Nat Rev Dis Primers* **8**, 52 (2022)

*See *amendments* at end of slide deck

Onasemnogene abeparvovec-xioi (ZOLGENSMA)

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Onasemnogene abeparvovec-xioi (ZOLGENSMA)

An AAV vector-based gene therapy

Mechanism of Action:

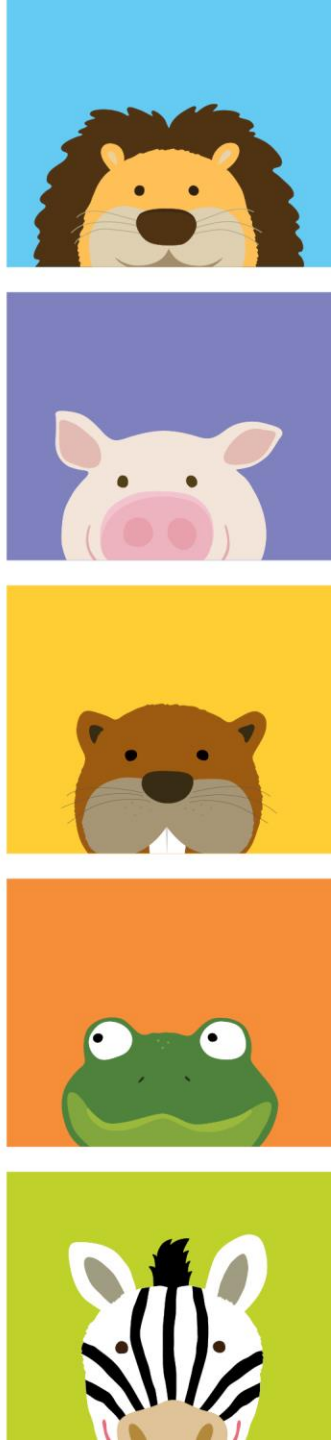
- A non-replicating, recombinant AAV serotype 9 vector which delivers a functional copy of the SMN1 gene to motor neurons

Indications:

- Patients with SMA with bi-allelic mutations in the *SMN1* gene
- Age requirement: <2 years old

Contraindications:

- None



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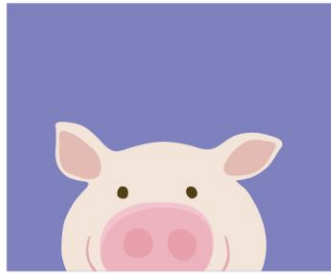
FDA. Zolgenmsa [package insert]. *Novartis Gene Therapies, Inc* Revised February 2025. Accessed September 13, 2025.

Onasemnogene abeparvovec-xioi (ZOLGENSMA)


Additional Eligibility Considerations:

- Presence of pre-existing anti-AAV9 antibodies ≥1:50
- Patient baseline for liver function, creatinine, and complete blood count
- Advancement of SMA disorder
- Administration to premature neonates prior to full-term gestational age

BBW:

- Serious liver injury and acute liver failure

Warnings / Precautions:

- May cause systemic immune response in patients with an active underlying infection
- May experience thrombotic microangiopathy and infusion-related reactions
- Potential risk of tumorigenicity

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FDA. Zolgenmsa [package insert]. *Novartis Gene Therapies, Inc* Revised February 2025. Accessed September 13, 2025.

Onasemnogene abeparvovec-xioi (ZOLGENSMA)

Adverse Reactions:

- ↑Aminotransferases, vomiting

Toxicities:

- Hepatotoxicity
- Potential cardiac toxicity and tumorigenicity

Monitoring Parameters:

- Signs and symptoms of hypersensitivity during and post infusion as necessary
- Liver function (e.g. liver enzymes) before infusion, then weekly x2 months, then every other week x1 month
- Platelet count before infusion, weekly x1 month post-infusion, then every other week x3 months
- Troponin-I post infusion as necessary
- Vital signs prior, during, and post infusion (>10% of “normal”)

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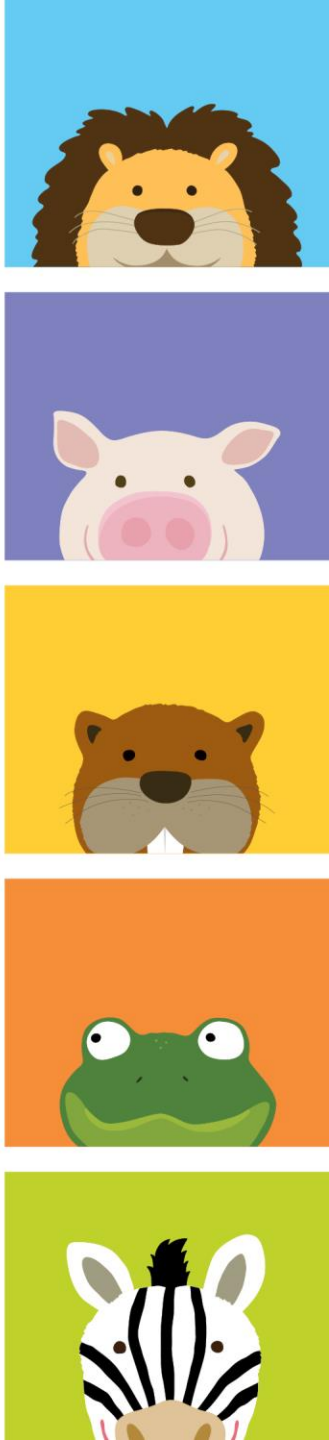


FDA. Zolgenmsa [package insert]. *Novartis Gene Therapies, Inc* Revised February 2025. Accessed September 13, 2025.

Onasemnogene abeparvovec-xioi (ZOLGENSMA)

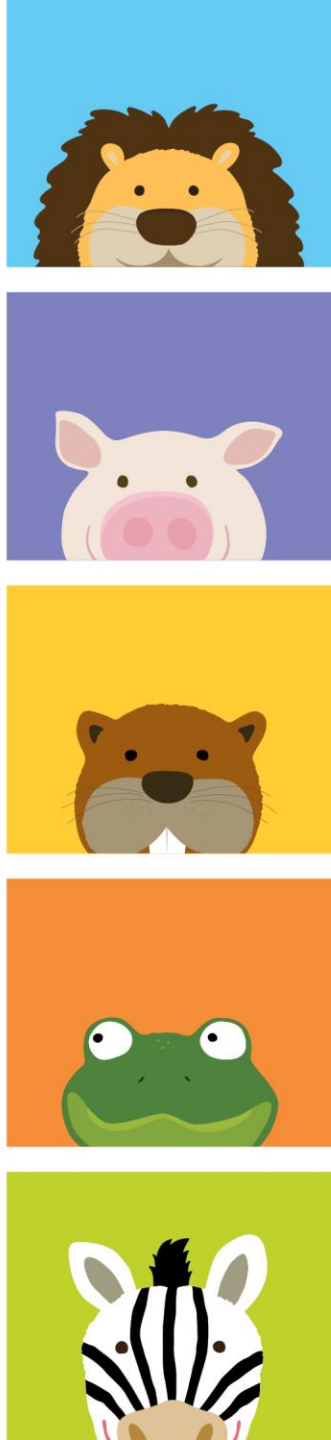
Dosing (in ABW):

- 1.1×10^{14} vg/kg
  - Calculated using the upper limit of the age weight range
- Packaged in kits containing 5.5mL and/or 8.3mL vials

Weight range (kg)	Dose volume (mL)
2.6-3	16.5
3.1-3.5	19.3
3.6-4	22
4.1-4.5	24.8
4.6-5	27.5

Administration:

- 1 day prior to infusion: administer prednisolone 1mg/kg/day (or equivalent)
  - Continue post-infusion: give a full dose for 30 days, followed by a 28-day taper
- Give Zolgensma via slow IV infusion over 60 minutes



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FDA. Zolgenmsa [package insert]. *Novartis Gene Therapies, Inc* Revised February 2025. Accessed September 13, 2025.

Onasemnogene abeparvovec-xioi (ZOLGENSMA)

Available as a therapy plan under AH

Procurement / Use Criteria:

- ONLY by neuromuscular specialists in SMA with qualifying mutations
- Involves “white bag” or “buy and bill” decision
- Requires agreement with payer prior to ordering

Storage & Handling:

- Shipped and delivered frozen (≤60°C) in 5.5mL and/or 8.3mL vials; do not refreeze
- Can be stable while refrigerated, upright for ≤14 days at 2-8°C; must be used within 8 hours once brought to room temperature
- Practice proper hygiene (e.g. hand washing) when in direct contact with gene therapy
- Place body fluids and waste in sealable bags x1 month post infusion

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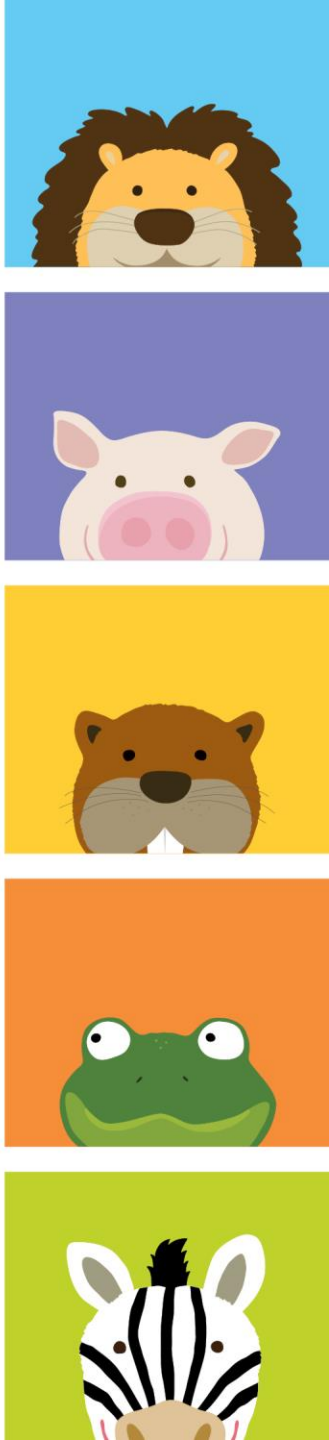


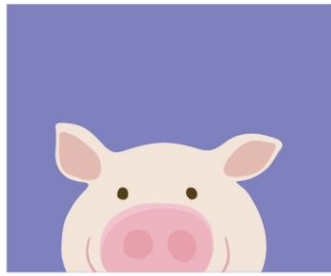
FDA. Zolgenmsa [package insert]. *Novartis Gene Therapies, Inc* Revised February 2025. Accessed September 13, 2025.

Onasemnogene abeparvovec-xioi (ZOLGENSMA)

- Cost considerations:

Zolgensma
~$2.4 million (WAC)

Total Annual Cost of Illness
~$324,000 per year (Type I)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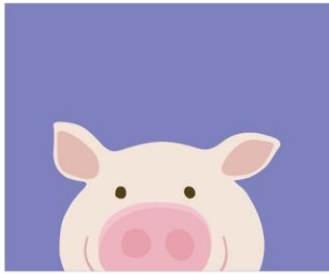
Landfeldt E, et al. *Appl Health Econ Health Policy*. 2021;19(4):501-520.

Onasemnogene abeparvovec-xioi Literature Review

Advocate Children's Hospital | Now part of ADVOCATEHEALTH

Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial

Purpose: Determine the safety and efficacy of onasemnogene abeparvovec for presymptomatic infants ≤6 weeks old with biallelic *SMN1* mutations


Inclusion Criteria

- Patients with pre-symptomatic SMA type I [i.e. 2 copies of *SMN2* gene (n≥14) OR
- Patients with pre-symptomatic SMA type II [i.e. 3 copies of *SMN2* gene (n≥12)]
- Patients ages ≤6 weeks old at administration of dose
- Gestational age: 35-42 weeks old
- ≥2kg at screening
- CMAP ≥2mV at baseline

Intervention

- Day prior to infusion: initially administered 1 mg/kg/day
  - Patients receiving dose in May 2019 and onwards: 2 mg/kg/day
- One-time IV infusion of onasemnogene abeparvovec-xioi at $1.1x10^{14}$ over ~60 minutes
- 48hrs post-infusion: 1 mg/kg/day (or 2mg/kg/day if dose given in May 2019 and onwards) followed by 1mg/kg/day for minimum of 30 days, then taper

Outcomes

- Primary:
  - Achieved sitting independently for ≥30 seconds at any visit up ≤18 months old
- Secondary:
  - Ability to stand independently by 18 months
  - Ability to walk independently by 18 months
  - Survival at 14 months old
  - Ability to thrive by 18 months
- Safety data

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Strauss KA, et al. *Nat Med*. 2022;28(7):1381-1389

Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial

		*Onasemnogene abeparvovec (n = 14)	97.5% CI	P-value
Primary Endpoint	**Ability to sit independently for >30 seconds at any visit up ≤18 months old, n (%)**	14 (100)	(77, 100)	<0.0001
Other Motor Milestones (WHO-MGRS)	**Ability to stand independently by 18 months old, n (%)**	10 (71.4)	(42, 92)	<0.0001
	Ability to walk independently by 18 months old, n (%)	10 (71.4)	(42, 92)	<0.0001

*Intention-to-treat population

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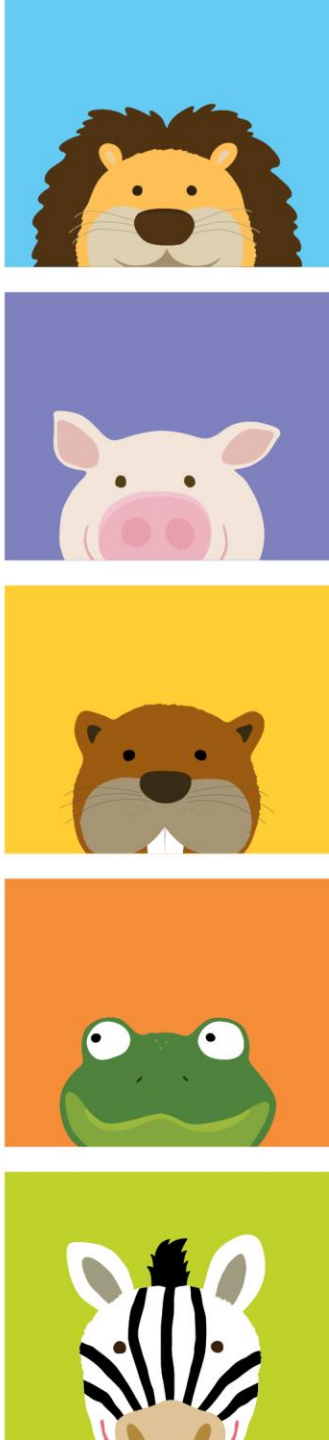
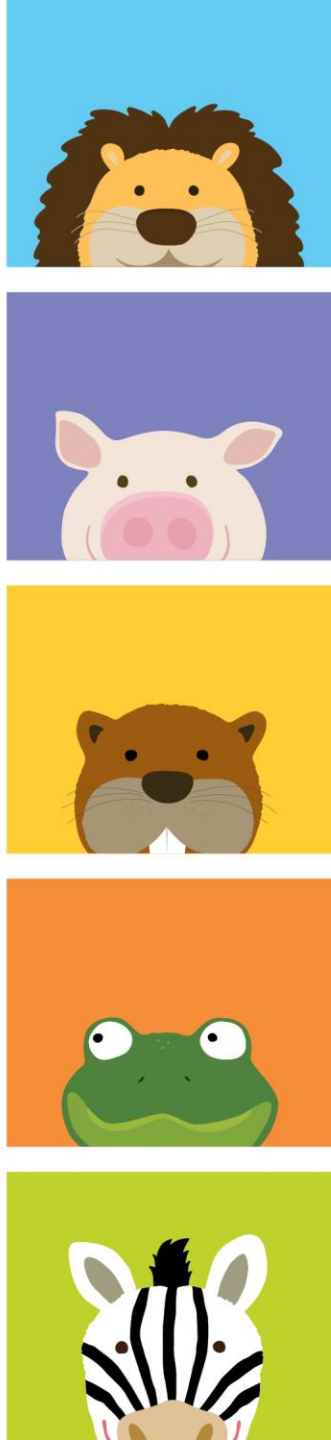
Strauss KA, et al. *Nat Med*. 2022;28(7):1381-1389



Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial

		Onasemnogene abeparvovec (*n = 14)	97.5% CI	P-value
Secondary Endpoints	**Survival at 14 months old, n (%)**	14 (100)	(77, 100)	<0.0001
	Ability to thrive by 18 months old, n (%)	12 (85.7)	(57, 98)	<0.0001

*Intention-to-treat population



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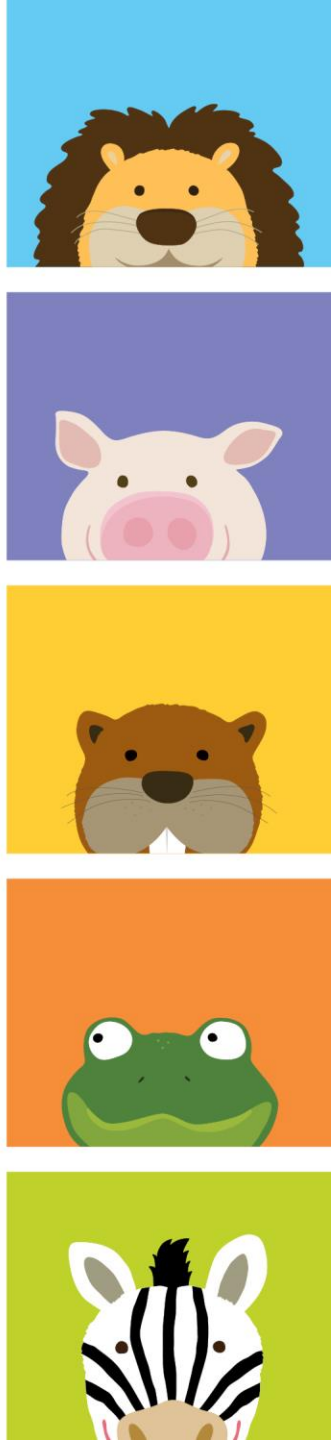
Strauss KA, et al. *Nat Med*. 2022;28(7):1381-1389

Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial

Incidence of Adverse Events, n (%)

	Onasemnogene abeparvovec (*n = 14)
Hepatotoxicity – any TEAE	3 (21.4)
Thrombocytopenia – any TEAE	3 (21.4)
Cardiac AE – any TEAE	2 (14.3)
Thrombotic microangiopathy – Any TEAE	2 (14.3)

*Safety population



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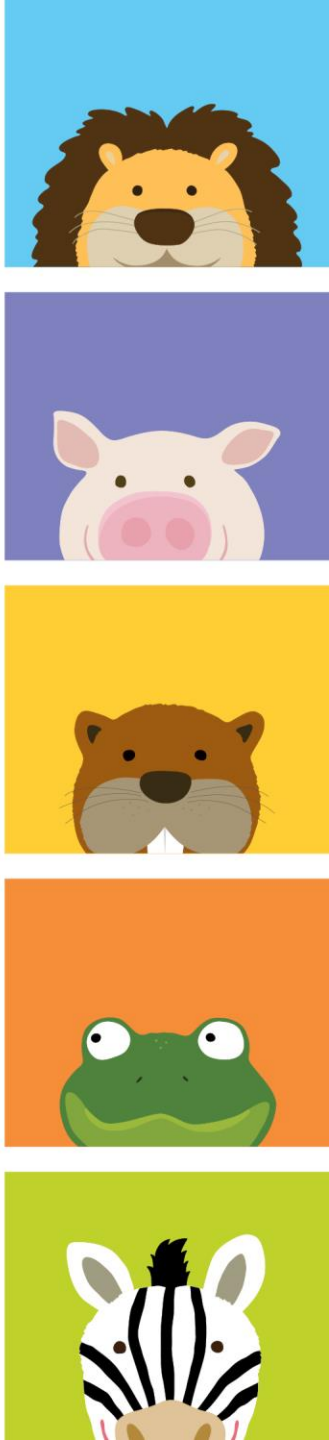

Conclusion

- Demonstrated efficacy and a favorable safety profile in presymptomatic infants
- Primary endpoint of patients being able to sit without additional support at any visit by 18-month-old was statistically significant (100% success, p <0.0001)

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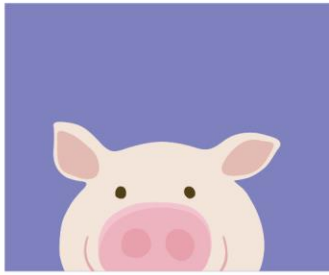
Strauss KA, et al. *Nat Med*. 2022;28(7):1381-1389

Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial

Purpose: Determine the safety and efficacy of onasemnogene abeparvovec for symptomatic infants ≤6 weeks old with biallelic *SMN1* mutations


Inclusion Criteria

- Patients with pre-symptomatic or symptomatic SMA type I (i.e. biallelic *SMN1* mutations and 1-2 copies of *SMN2*
- Patients ages ≤6 months old at administration of infusion
- Must be up to date with childhood vaccinations
- Performed swallowing test prior to infusion

Intervention

- Day prior to infusion: initially administered 1 mg/kg/day prednisolone
- One-time IV infusion of onasemnogene abeparvovec-xioi at $1.1x10^{14}$ over 30-60 minutes via peripheral vein
- Post infusion: continue 1 mg/kg/day prednisolone for at least 30 days

Outcomes

- Primary:
  - Proportion of patients able to sit independently ≥30 seconds at 18 months old visit
  - Survival at 14 months old
- Secondary:
  - Ability to thrive at 18 months old
  - Independence from ventilatory support at 18 months old
  - Achievement of motor milestones
- Safety data

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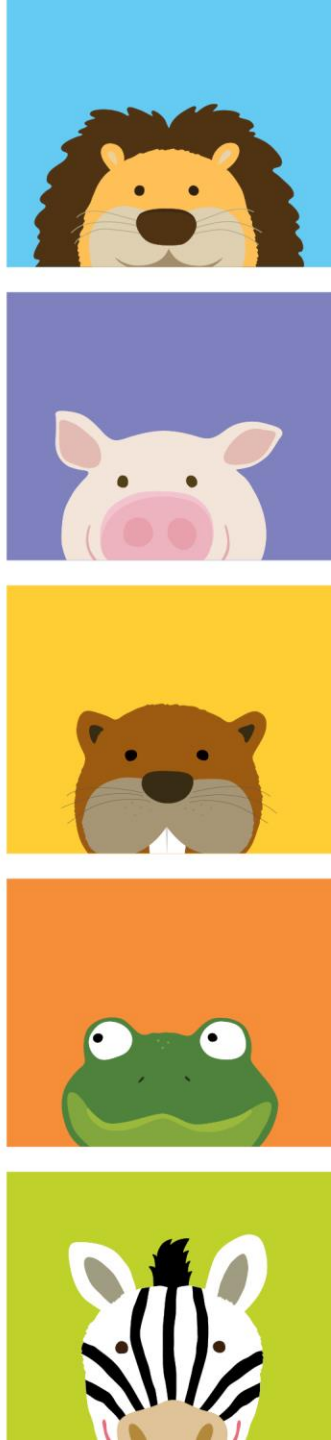
Day JW, et al. *Lancet Neurol*. 2021 Apr;20(4):284-293

Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial

		Onasemnogene abeparvovec (n = 22)	CI	Untreated (n=23)	P-value
Co-primary Endpoints	**Ability to sit independently for >30 seconds at any visit up ≤18 months old, n (%)**	13 (59.1)	97.5% CI (36-100)	0 (0)	<0.0001
	Survival at age 14 months, n (%)	20 (90.1)	95% CI (42, 92)	6 (26.1)	<0.0001



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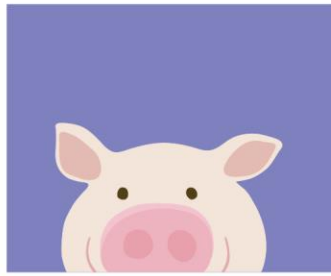
		Onasemnogene abeparvovec (n = 22)	CI	P-value
Secondary Endpoints	**Ability to thrive at 18 months old, n (%)**	9 (40.9)	97.5% CI (21-100)	<0.0001
	No need for ventilation support at 18 months old, n (%)	18 (81.8)	97.5% CI (59.7-100)	<0.0001
Exploratory Endpoint	**Achievement of motor milestones, n (%)**	19 (86.4)	-	-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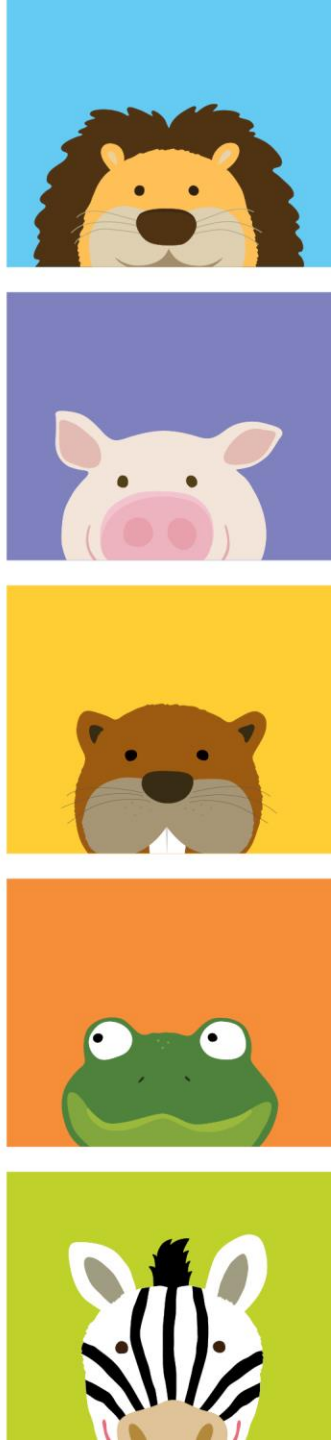
Day JW, et al. *Lancet Neurol*. 2021 Apr;20(4):284-293

Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial

Incidence of Adverse Events, n (%)

	Onasemnogene abeparvovec (n = 22)
Hepatotoxicity	7 (31.8)
Hematologic	8 (36.4)
Cardiovascular	4 (18.2)
Neurologic	5 (22.7)



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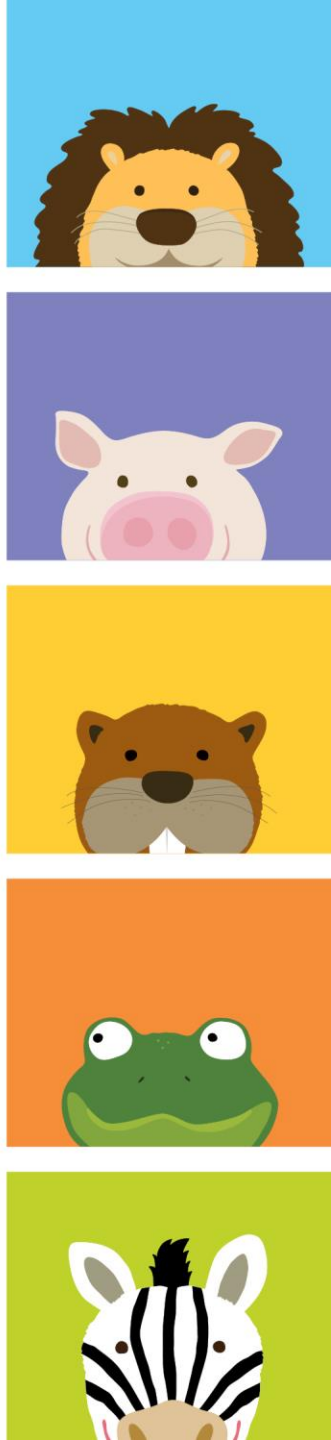
Day JW, et al. *Lancet Neurol*. 2021 Apr;20(4):284-293

Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial

Conclusion

- Demonstrated efficacy in symptomatic SMA type I patients <6 months old
- Showed a favorable benefit-risk profile, with common adverse events seen (e.g. ↑aminotransferase) that can be manageable with monitoring and course of corticosteroids



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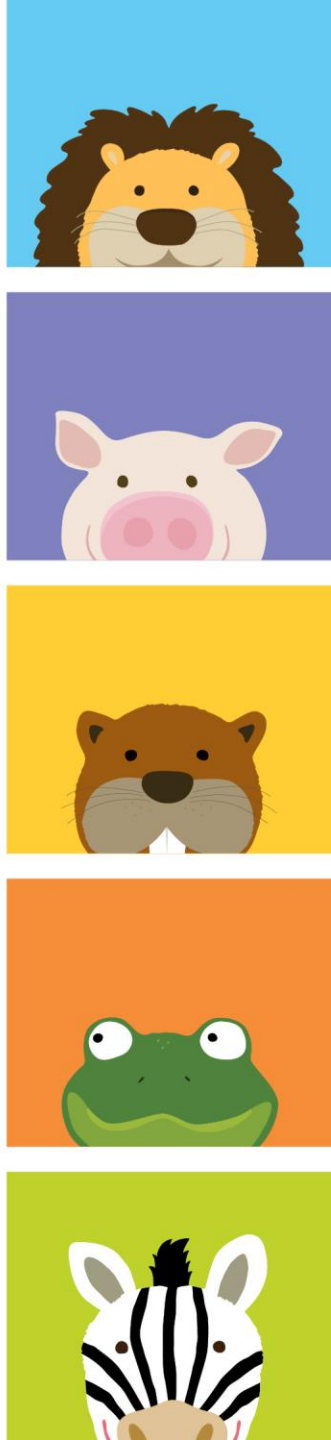
Day JW, et al. *Lancet Neurol*. 2021 Apr;20(4):284-293

Assessment Question #2

- A parent of a 6-week-old child with confirmed SMA type I is being educated on adverse reactions associated with Onasemnogene abeparvovec (*Zolgensma*). Which of the following adverse reaction is associated with this gene therapy?
  - A) Febrile neutropenia
  - B) Elevated aminotransferases
  - C) Myocarditis
  - D) Lymphopenia



Sickle Cell Disease

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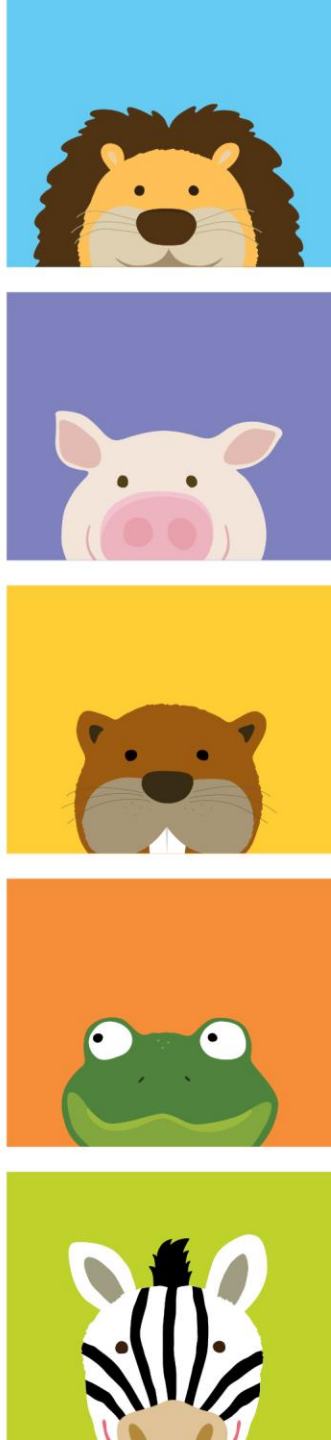
What is SCD?

An inherited red blood cell disorder that causes a genetic mutation in the gene which encodes hemoglobin, producing HbS

- Characterized by its sickle-shape and recurrent vaso-occlusive crises, vascular damage, chronic hemolysis, end organ damage

Affects 100,000 individuals

Average lifespan with optimal care: ~54 years



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Kavanagh P, et al. *JAMA*. 2022;328(1):57-68.

What is SCD?

- Progression of disease:

Infancy & Childhood

- Delayed growth

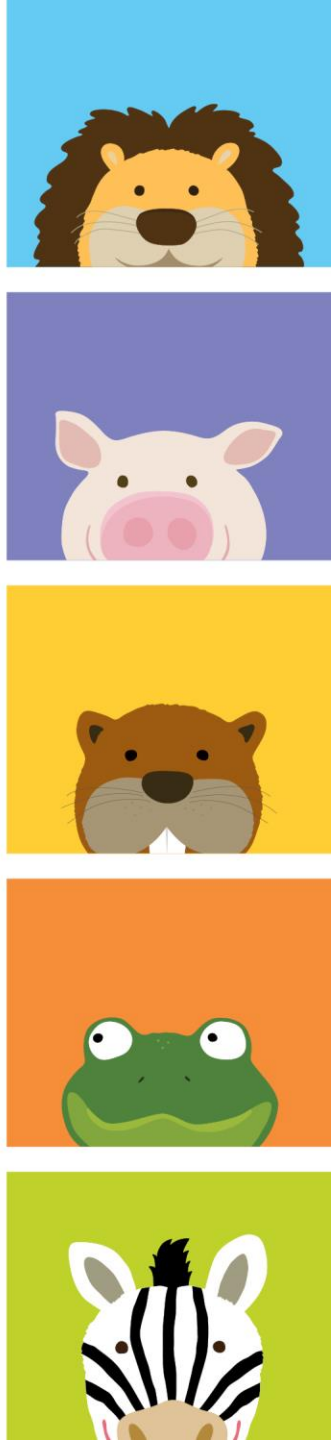
Adolescence

- Delayed puberty

Adulthood

- Hemorrhagic stroke
- Pulmonary hypertension
- Reproductive complications (e.g. ↑pregnancy complications)
- Leg ulcers

- <u>Complications throughout lifespan:</u>
  - Acute pain
  - Acute chest syndrome
  - Ischemic stroke



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Kavanagh P, et al. *JAMA*. 2022;328(1):57-68.

Current Management

Non-pharmacological Management

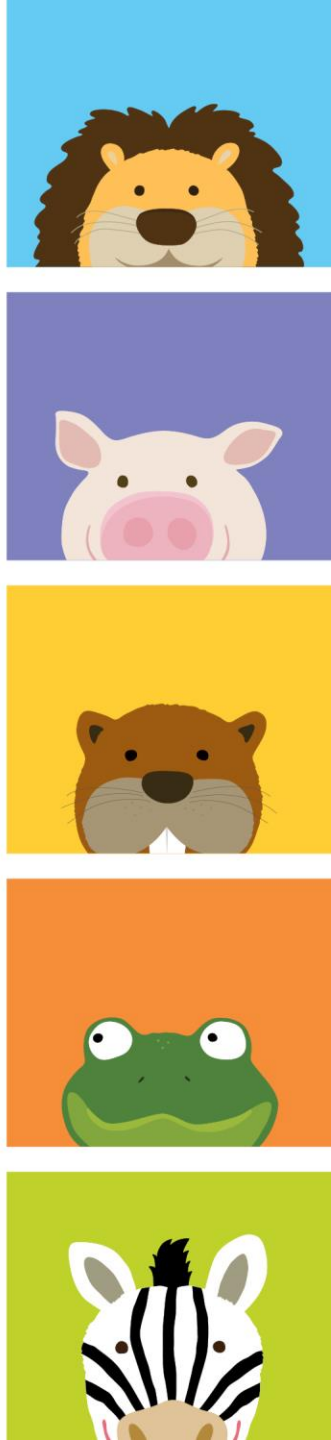
- Blood transfusions
- Bone marrow transplant

Pharmacological Management

- Pain management
  - Mild-moderate pain: non-opioid therapy (e.g. acetaminophen or NSAIDs)
  - Severe: parenteral opioids (i.e. IV morphine)
- Hydroxyurea
- L-glutamine
- Iron chelation (e.g. deferasirox)

Gene Therapy

- AH available gene therapy to consider: *Exagamglogene autotemcel*



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Kavanagh P, et al. *JAMA*. 2022;328(1):57-68.

Exagamglogene autotemcel (CASGEVY)

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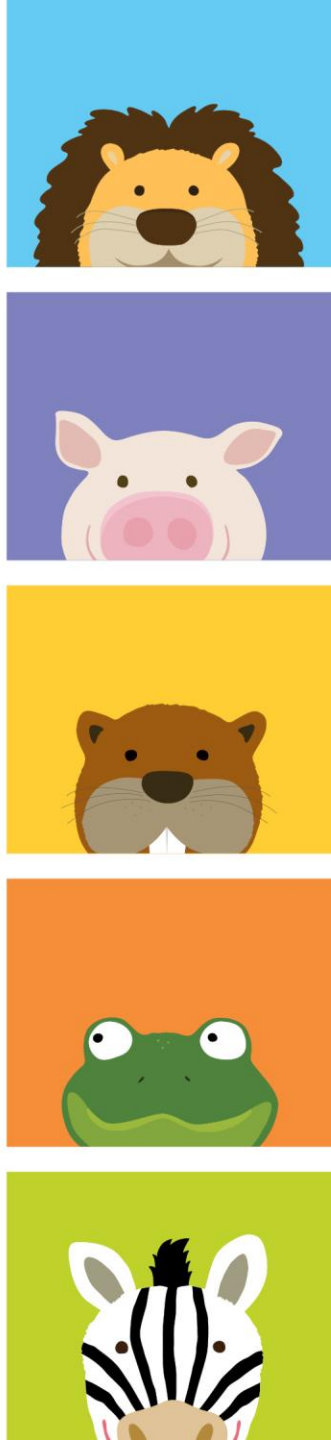
Exagamglogene autotemcel (CASGEVY)

A non-viral, ex-vivo autologous CD34+ hematopoietic stem cell-based gene therapy edited by CRISPR/Cas9

Mechanism of Action:

- Creates a DNA double-strand break at the *BCL11A* gene erythroid-specific enhancer region, allowing reduced expression of the *BCL11A* gene → increased HbF production and γ-globin expression
  - ↑HbF, ↓ HbS = prevention of vaso-occlusive pain crises
  - Improved imbalance in α-globin to non-α-globin → increased Hgb levels → prevents the need for regular blood transfusions



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FDA. Casgevy [package insert]. *Vertex Pharmaceuticals, Inc*. Revised December 2023. Accessed September 17, 2025.

Exagamglogene autotemcel (CASGEVY)

Indications:

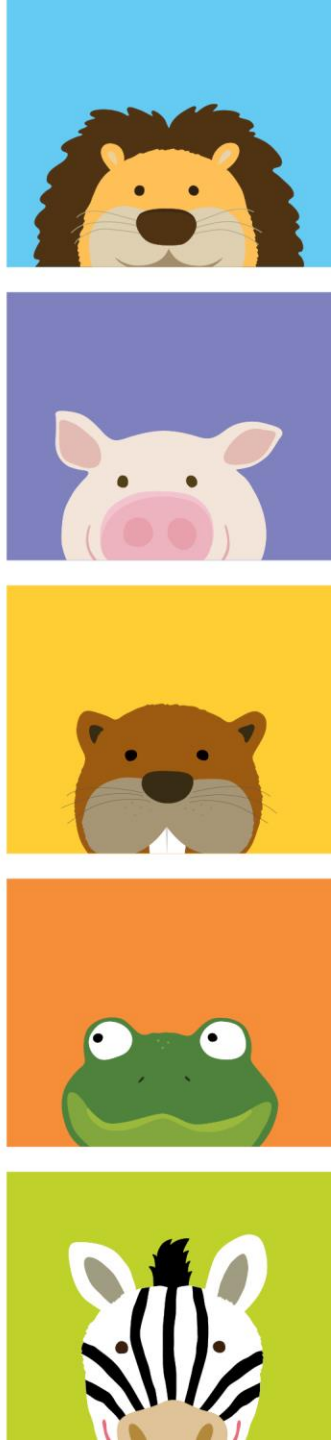
- Patients with SCD with recurrent vaso-occlusive crises
- Patients with SCD with recurrent vaso-occlusive crises and TDT
- Age requirement: 12 years old

Contraindications:

- None

Additional Eligibility Considerations:

- The use of hydroxyurea, voxelotor, crizanlizumab, and iron chelators should be discontinued prior to initiation
  - Hydroxyurea/Voxelotor*/Crizanlizumab : discontinue ≥8 weeks prior to start of mobilization and conditioning
  - Iron chelators: discontinue ≥7 days prior to initiation of myeloablative conditioning
  - Women who are pregnant or breastfeeding



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*See *amendments* at end of slide deck

FDA. Casgevy [package insert]. *Vertex Pharmaceuticals, Inc*. Revised December 2023. Accessed September 17, 2025.

Exagamglogene autotemcel (CASGEVY)

Additional Eligibility Considerations (Continued):

- A confirmed, negative pregnancy test must be documented prior to each mobilization cycle and myeloablative conditioning

Warnings / Precautions:

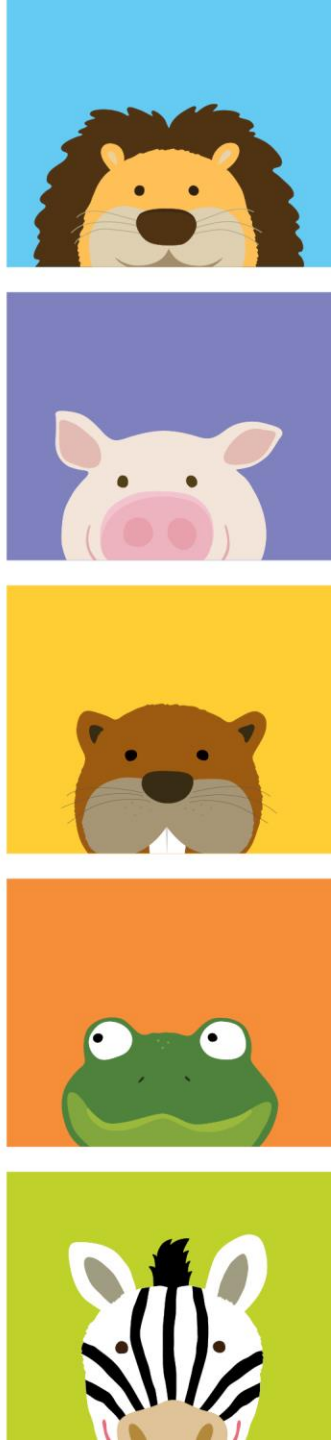
- Can cause neutrophil engraftment failure, delayed platelet engraftment, and hypersensitivity reactions (e.g. anaphylaxis)
- Can cause laboratory abnormalities, including thrombocytopenia, neutropenia, leukemia, anemia, and lymphopenia
- Risk of off-target genome editing

Adverse Reactions:

- Mucositis, febrile neutropenia, anemia, thrombocytopenia
- More veno-occlusive liver disease in TDT

Toxicities:

- Unknown



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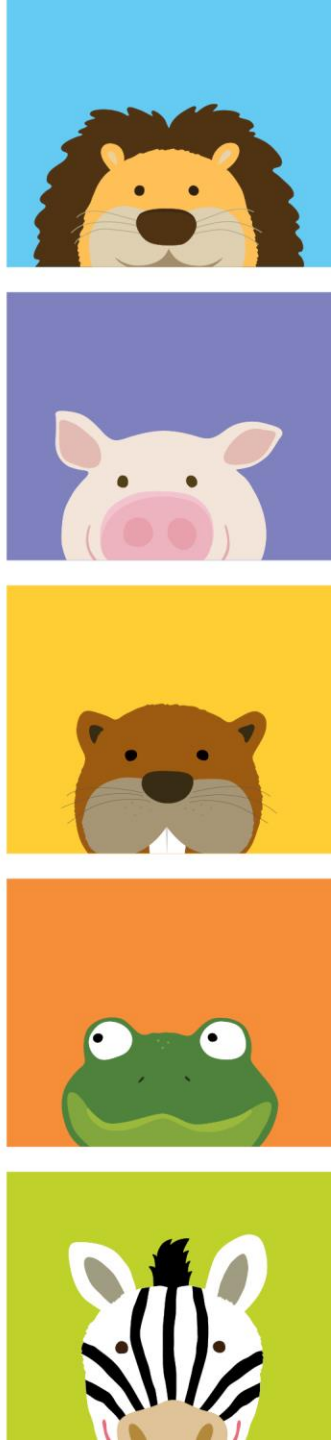
Exagamglogene autotemcel (CASGEVY)

Monitoring Parameters:

- Complete blood count (absolute neutrophil count, platelet, Hgb, WBC)
- Hypersensitivity reactions pre- and post-infusion

Administration

- SCD: 8 weeks prior, transfuse patient to maintain HbS level to <30% of total Hgb, maintaining a Hgb concentration of ≤11g/dL
- TDT: 8 weeks prior, transfuse patient to maintain a Hgb concentration of ≥11g/dL
- Administer gene therapy via IVP through central catheter within 20 minutes of being thawed
  - If >1 vial is needed, complete administration of first vial prior to thawing the next vial
  - Administer each vial's content as IVP, being mindful to not exceed 2.6mL/kg within one hour
- Flush primary line with normal saline



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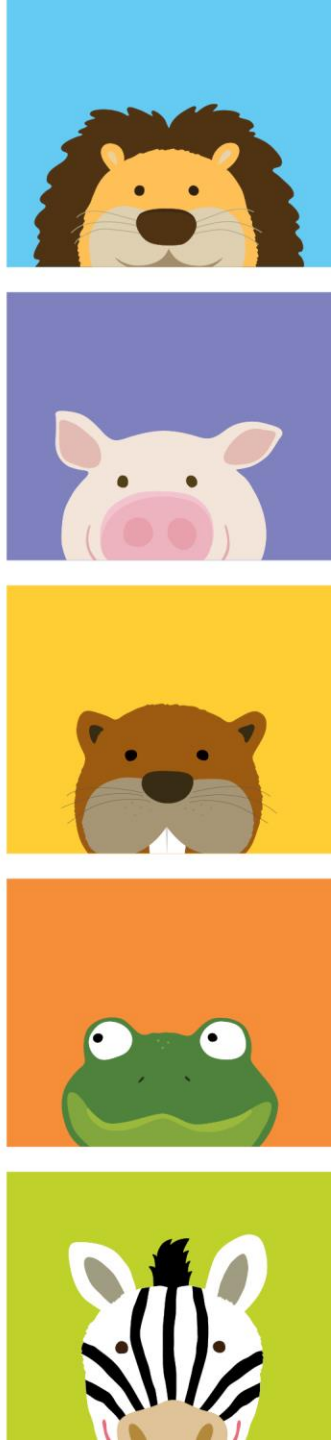
FDA. Casgevy [package insert]. *Vertex Pharmaceuticals, Inc*. Revised December 2023. Accessed September 17, 2025.

Exagamglogene autotemcel (CASGEVY)

1. • Stop medications, like hydroxyurea, or chelation and transfuse patient
2. • Administer medication (e.g. plerixafor) for stem cell mobilization and collect stem cells
   • Set aside extra “rescue” stem cells
3. • Stem cells are sent to a manufacturing lab to undergo modification
4. • Receive shipment to facility, utilizing 2 patient identifiers
   • Store in cryo freezer
5. • Begin conditioning (i.e. chemotherapy) and wait 48hrs to 7 days post-chemo
6. • Thaw vials of gene therapy one at a time, then infuse IVP and flush with normal saline; repeat for total number of vials in kit
7. • Post-treatment monitoring



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CASGEVY® Brochure | CASGEVY® (exagamglogene autotemcel). *Vertex Pharmaceuticals, Inc.* 2025. Accessed September 21, 2025.

Exagamglogene autotemcel (CASGEVY)

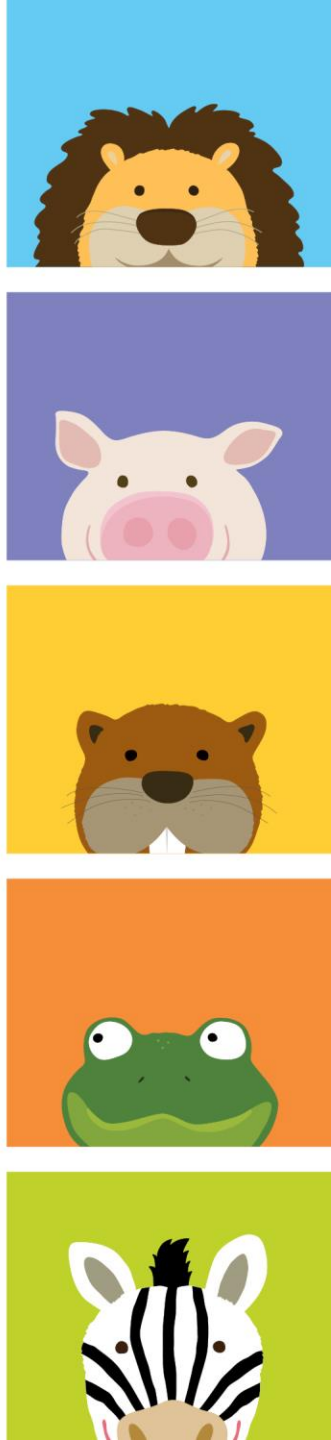
Should be ordered using official therapy plan or beacon plan under AH

Procurement / Use Criteria:

- ONLY for pediatric facilities that offer hematopoietic cell transplantation and sickle cell program
- Recommend using payer provided medication
- Involves “white bag” or “buy and bill” decision

Storage & Handling*:

- Shipped and delivered frozen in a vapor phase of liquid nitrogen shipper at ≤ -135 °C (≤ -211 °F)
- Patient identifiers must be confirmed
- Thaw contents in a water bath and infuse within 20 minutes
- Bodily fluids and/or waste must be handled in accordance with local biosafety guidelines



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*See *amendments* at end of slide deck

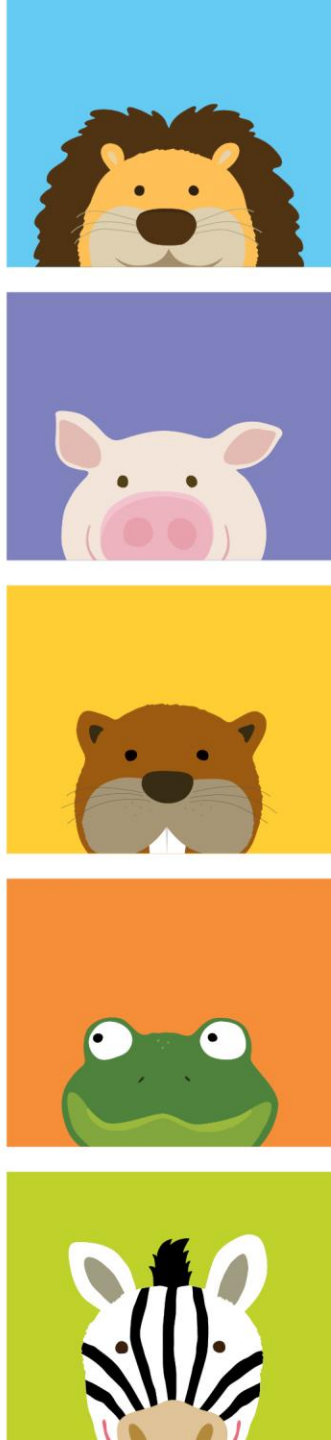
FDA. Casgevy [package insert]. *Vertex Pharmaceuticals, Inc*. Revised December 2023. Accessed September 17, 2025.

Exagamglogene autotemcel (CASGEVY)

- Cost considerations:

Casgevy
~$2.4 million (WAC)

Total Annual Cost of Illness
~$45,000 per year



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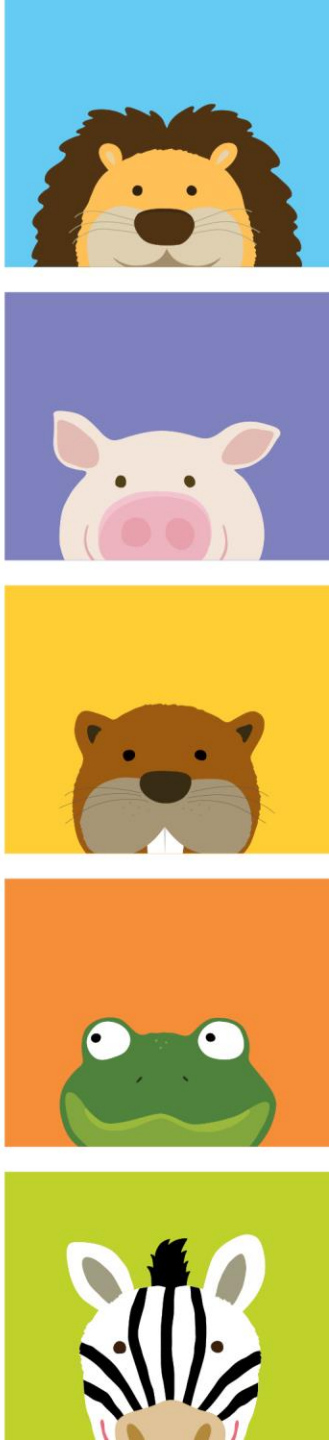
Johnson KM, et al. *Blood Advances*. 2022;7(3).

Assessment Question #3

- A pharmacist is overseeing the preparation of exagamglogene autotemcel (CASEGEVY). Knowing the pharmacist's role in managing/handling this product, which of the following is correct?
  - A) Pharmacists involved in receiving shipment of the gene therapy are required to confirm two patient identifiers.
  - B) Pharmacists involved in receiving shipment of the gene therapy should place this product immediately in the refrigerator.
  - C) Since the product is packaged in two vials, the pharmacist must communicate to the IV technician that both vials should be thawed at the same time.
  - D) The pharmacist should tell the technician that the BUD of the product should be labeled as 24hrs.



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Exagamglogene autotemcel Literature Review

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Exagamglogene Autotemcel for Severe Sickle Cell Disease
(CLIMB SCD-121 Study Group)

Purpose: Determine the safety and efficacy of exagamglogene autotemcel for pediatric and adult patients with sickle cell disease.

Inclusion Criteria

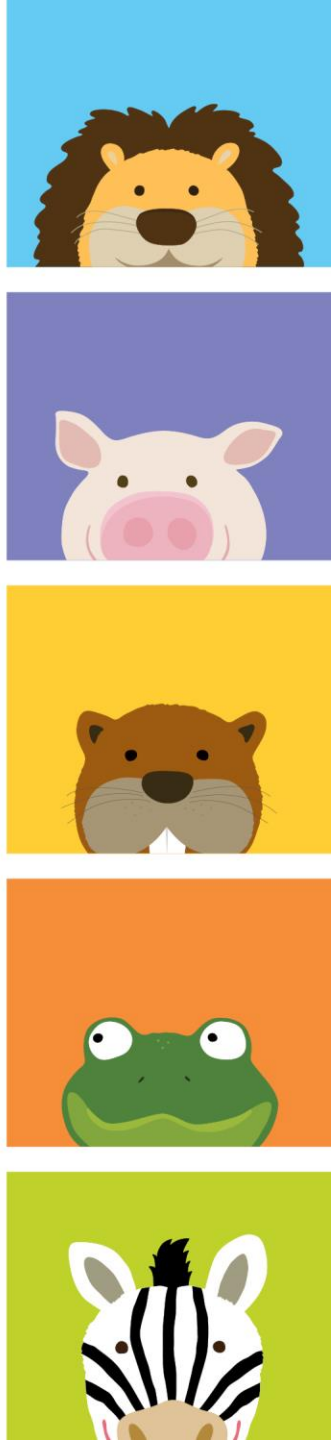
- Patients with diagnosed SCD defined by having documented severe SCD genotype, history of ≥2 severe vaso occlusive crises/year for the 2 previous years prior to enrollments
- Patients ages 12-35 years old at administration of dose

Intervention

- One infusion of CTX001 (autologous CD34+ hematopoietic stem cell-based gene therapy modified with CRISPR/Cas9)

Outcomes

- Primary:
  - No severe vaso-occlusive crises for ≥12 consecutive months
- Secondary:
  - No inpatient hospitalization for severe vaso-occlusive crises for at ≥12 consecutive months
  - No severe vaso-occlusive crises for ≥9 consecutive months
- Safety data



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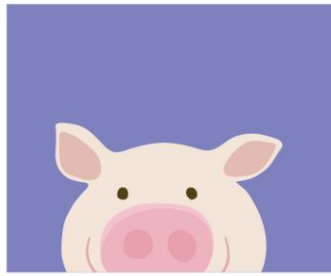
Frangoul H, et al. *N Engl J Med*. 2024;390(18):1649-1662.

Exagamglogene Autotemcel for Severe Sickle Cell Disease
(CLIMB SCD-121 Study Group)

		Exagamglogene Autotemcel (n = 30)	97.5% CI	P-value
Primary Endpoint	**No severe vaso-occlusive crises for ≥12 consecutive months, n (%)**	29 (96.7)	(83, 100)	<0.001

*Primary efficacy population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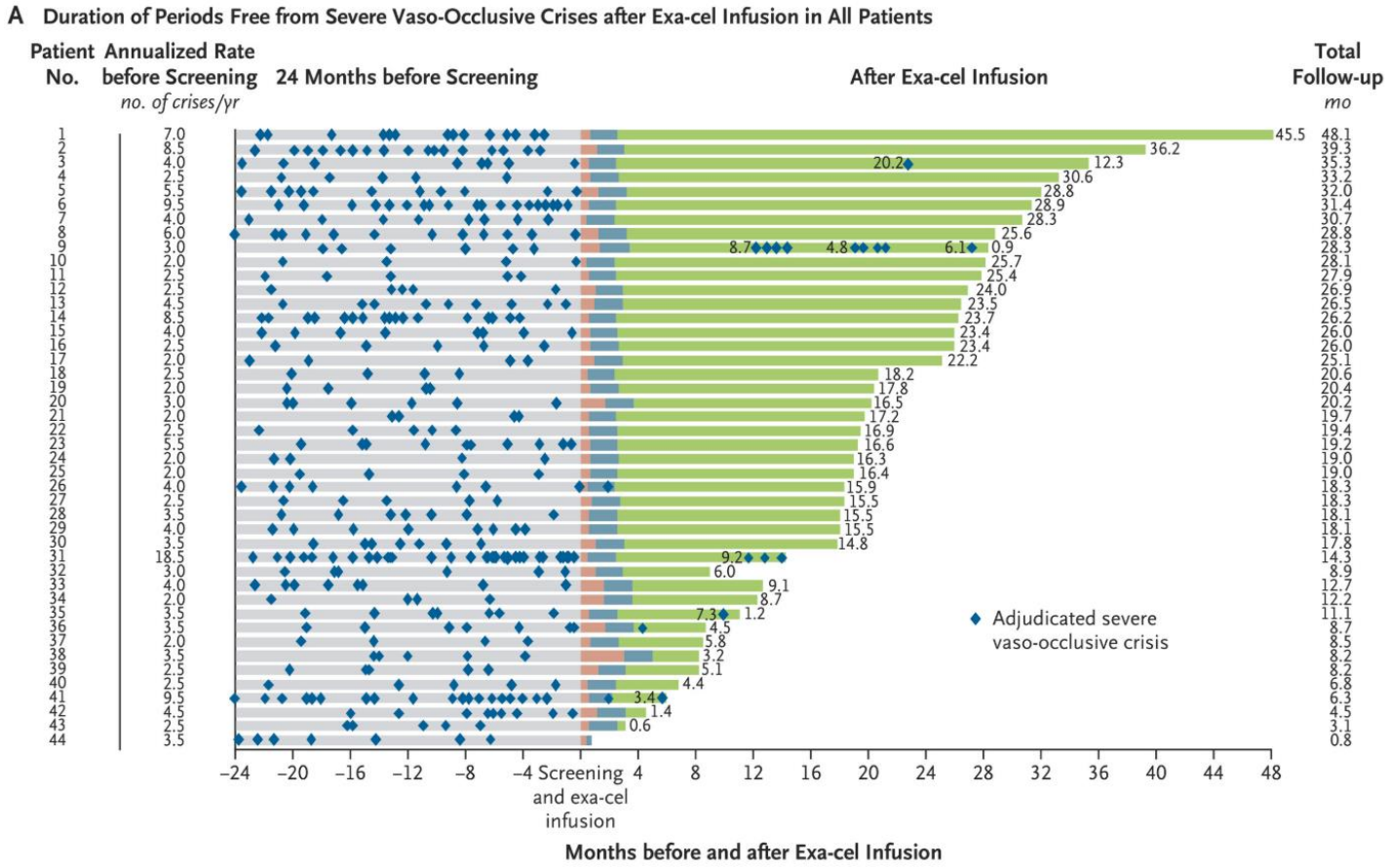
(CLIMB SCD-121 Study Group)



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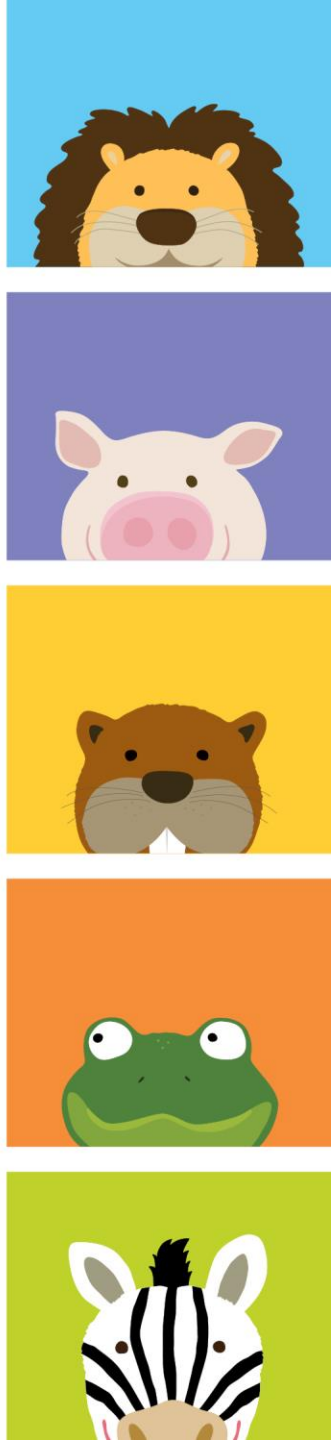
Exagamglogene Autotemcel for Severe Sickle Cell Disease
(CLIMB SCD-121 Study Group)

		Exagamglogene Autotemcel	97.5% CI	P-value
Secondary Endpoints	**No inpatient hospitalization for severe vaso-occlusive crises for at ≥12 consecutive months, n (%)**	30/30 (100)	(88, 100)	<0.001
	No severe vaso-occlusive crises for ≥9 consecutive months, n (%)	31/32 (96.9)	(84, 100)	<0.001

*Early efficacy population



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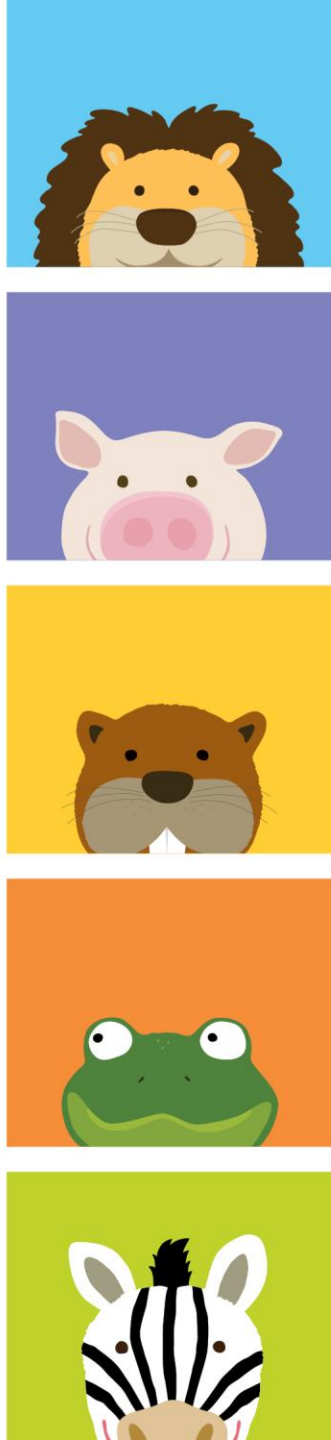
Exagamglogene Autotemcel for Severe Sickle Cell Disease
(CLIMB SCD-121 Study Group)

Incidence of Adverse Events, n (%)	
	Exagamglogene Autotemcel (n=44)
Grade 3 or 4 ADE	42 (95)
Stomatitis	24 (55)
Febrile neutropenia	21 (48)
PLT count decrease	21 (48)



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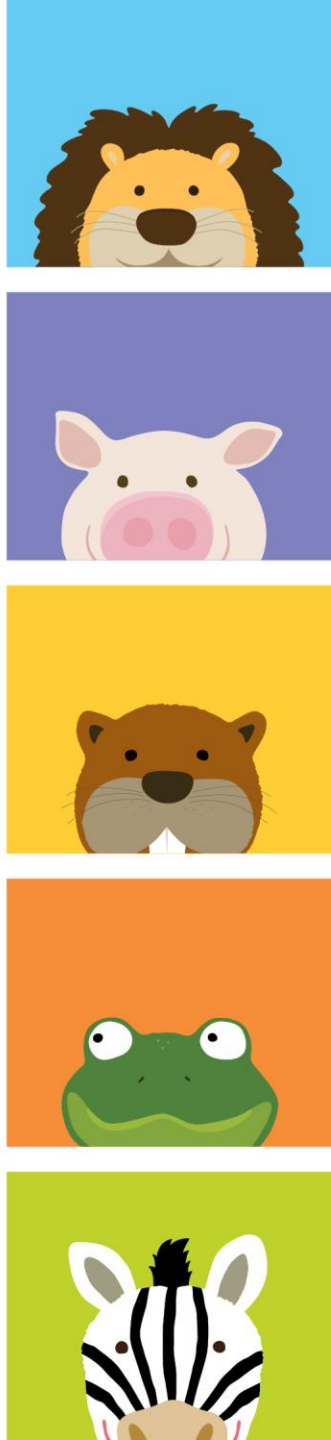
Exagamglogene Autotemcel for Severe Sickle Cell Disease
(CLIMB SCD-121 Study Group)

Conclusion

- Primary endpoint of having no severe vaso-occlusive crises for >12 consecutive months was met and demonstrated significant improvement
- Safety profile of exa-cel was consistent with autologous Hematopoietic stem and progenitor cell (HSPC) transplantation and myeloablative busulfan conditioning



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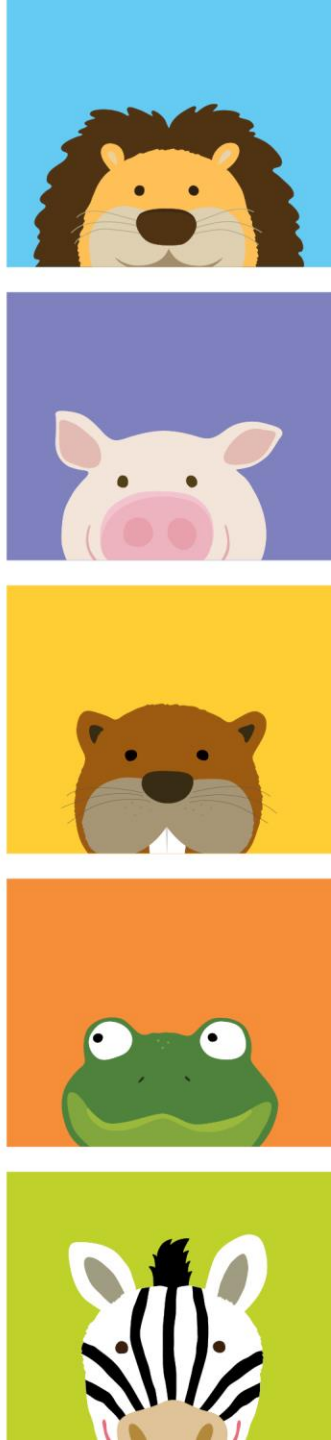
More Available Gene Therapies

FDA Approved Pediatric Gene Therapies

Gene Therapy	Indication	Age Requirements
Eladocagene exuparvovec-tneq (KEBILIDI)	Aromatic L amino acid decarboxylase (AADC) deficiency	≥16 months old (16mo - 10yr olds studied)
Tisagenlecleucel (KYMRIAH)	Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)	<25 years old (2 - 17yrs old studied)
Atidarsagene autotemcel (LENMELDY)	Pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ), OR early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD)	≥8 months (8mo - <12yrs studied)
Voretigene neparvovec-rzyl (LUXTURNA)	Confirmed biallelic RPE65 mutation-associated retinal dystrophy	>4 years old (not explicitly specified) (4 - <17yrs old studied)
Lovotibeglogene autotemcel (LYFGENIA)	Sickle cell disease	≥12 years old (12-<18yrs old studied)
Elivaldogene autotemcel (SKYSONA)	Active cerebral adrenoleukodystrophy (CALD)	4 - 17 years old
Beremagene geperpavec-svdt (VYJUVEK)	Dystrophic epidermolysis bullosa	≥6 months old (≤16yr olds studied)
Prademagene zamikeracel (ZEVASKYN)	Wounds with recessive dystrophic epidermolysis bullosa (RDEB)	≥6 years old (6 and 16yr olds studied)
Betibeglogene autotemcel (ZYNTEGLO)	β-thalassemia	≥4 - <18 years old (≤18yr olds studied)



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FDA. Approved Cellular and Gene Therapy Products. Updated August 15, 2025.

Patient Case Example

Patient Case Example

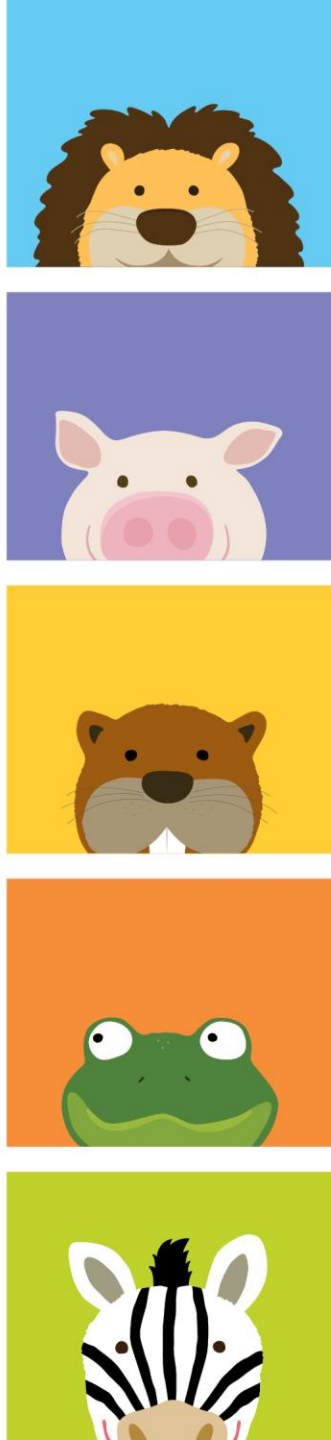
Meet Baby S: A now 16-month-old patient who was diagnosed with SMA at 1-week-old based on their newborn screening

- Genetic workup later indicated 0 SMN1 genes and 2 SMN2 genes
- AAV9 antibody level: <1.25

2-weeks-old: Motor exam was completed and indicated no abnormalities (i.e. normal neurologic exam)

~1-month-old: Plan for onasemnogene abeparvovec-xioi (ZOLGENSMA) therapy (weight = 5kg)

- Day prior to receiving gene therapy + for next 30 days: Pt received prednisolone 1mg/kg (= 5mg/day)
- Day of receiving gene therapy: 1.1x10^14 vg/kg (= 24.8mL kit)
  - No adverse reactions noted during or after infusion



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Patient Case Example

~5-months-old: Telephone call

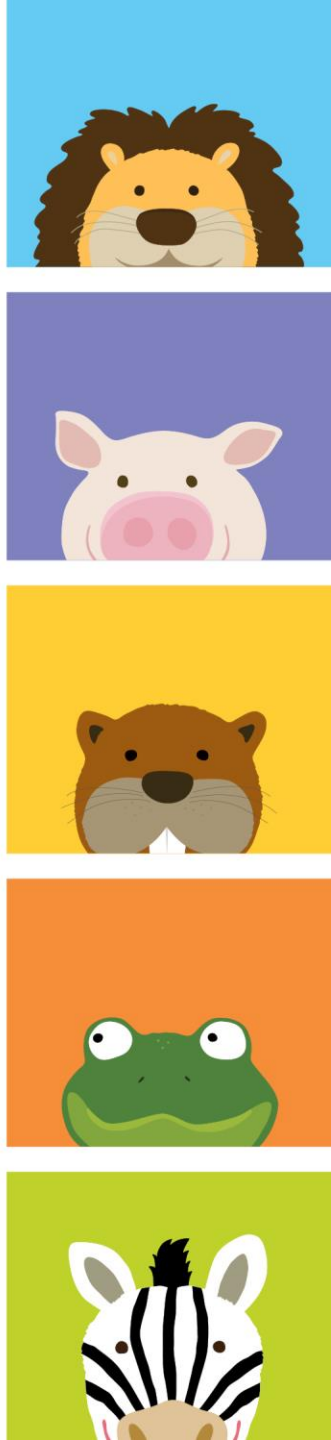
Patient was getting PT/OT every other week

5-months-old: Office visit

Meeting normal milestones; normal neurologic exam

14-months-old: Office visit

Making good progress; normal neurologic exam



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Patient Case Example

	Alanine Aminotransferase (ALT)	Total Bilirubin	Partial Thromboplastin Time (PTT)
1-week-old	21	3.8	41
1-month-old	27	0.6	
2-months-old	25	0.5	
4-months-old			

	International Normalized Ratio (INR)	Platelet	Troponin-I
1-week-old	1.1	578	71
1-month-old	1.1	443	52
2-months-old	1.1	510	76
4-months-old	1.4		

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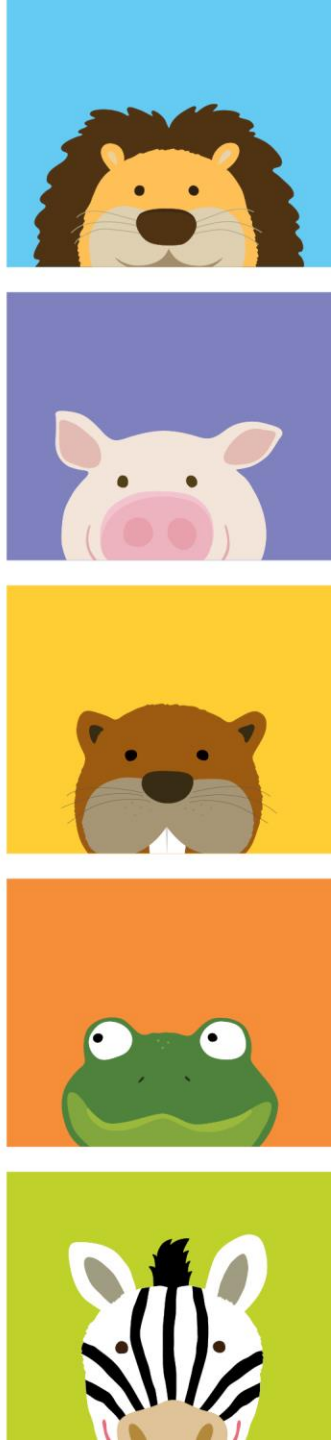

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References

1. Kaufmann KB, Büning H, Galy A, Schambach A, Grez M. Gene therapy on the move. *EMBO Mol Med*. 2013;5(11):1642-1661. doi:10.1002/emmm.201202287
2. Chancellor D, Barrett D, Nguyen-Jatkoe L, Millington S, Eckhardt F. The state of cell and gene therapy in 2023. *Mol Ther*. 2023;31(12):3376-3388. doi:10.1016/j.ymthe.2023.11.001
3. Li X, Le Y, Zhang Z, Nian X, Liu B, Yang X. Viral Vector-Based Gene Therapy. *Int J Mol Sci*. 2023;24(9):7736. Published 2023 Apr 23. doi:10.3390/ijms24097736
4. Emborg ME, Metzger JM, D'Amour K, et al. Advantages and challenges of using allogeneic vs. autologous sources for neuronal cell replacement in parkinson's disease: Insights from non-human primate studies. *Brain Research Bulletin*. 2025;224:111297. doi:10.1016/j.brainresbull.2025.111297
5. Approved Cellular and Gene Therapy Products. U.S Food & Drug Administration. Updated August 15, 2025. Accessed September 13, 2025. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products
6. Venugopal V, Pavlakis S. Duchenne Muscular Dystrophy. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482346/
7. Elevidys [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; U.S. Food & Drug Administration. Revised June 2024. Accessed September 13, 2025. https://www.fda.gov/media/184855/download?attachment
8. Landfeldt E, Lindgren P, Bell CF, et al. The burden of Duchenne muscular dystrophy: an international, cross-sectional study. *Neurology*. 2014;83(6):529-536. doi:10.1212/WNL.0000000000000669
9. Mendell JR, Muntoni F, McDonald CM, et al. AAV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial. *Nat Med*. 2025;31(1):332-341. doi:10.1038/s41591-024-03304-z
10. FDA Requests Sarepta Therapeutics Suspend Distribution of Elevidys and Places Clinical Trials on Hold for Multiple Gene Therapy Products Following 3 Deaths. U.S Food & Drug Administration. July 18, 2025. Accessed September 21, 2025. https://www.fda.gov/news-events/press-announcements/fda-requests-sarepta-therapeutics-suspend-distribution-elevidys-and-places-clinical-trials-hold
11. FDA Recommends Removal of Voluntary Hold for Elevidys for Ambulatory Patients. U.S Food & Drug Administration. July 28, 2025. Accessed September 21, 2025. https://www.fda.gov/news-events/press-announcements/fda-recommends-removal-voluntary-hold-elevidys-ambulatory-patients
12. Burr P, Reddivari AKR. Spinal Muscle Atrophy. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560687/
13. Mercuri, E., Sumner, C.J., Muntoni, F. *et al.* Spinal muscular atrophy. *Nat Rev Dis Primers* 8, 52 (2022). https://doi.org/10.1038/s41572-022-00380-8
14. Zolgenmsa [package insert]. East Hanover, NJ: Novartis Gene Therapies, Inc.; U.S. Food & Drug Administration. Revised February 2025. Accessed September 13, 2025. https://www.fda.gov/media/184855/download
15. Landfeldt E, Pechmann A, McMillan HJ, Lochmüller H, Sejersen T. Costs of Illness of Spinal Muscular Atrophy: A Systematic Review. *Appl Health Econ Health Policy*. 2021;19(4):501-520. doi:10.1007/s40258-020-00624-2
16. Strauss KA, Farrar MA, Muntoni F, et al. Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial. *Nat Med*. 2022;28(7):1381-1389. doi:10.1038/s41591-022-01866-4
17. Day JW, Finkel RS, Chiriboga CA, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial. *Lancet Neurol*. 2021;20(4):284-293. doi:10.1016/S1474-4422(21)00001-6
18. Kavanagh PL, Fasipe TA, Wun T. Sickle Cell Disease: A Review. *JAMA*. 2022;328(1):57-68. doi:10.1001/jama.2022.10233
19. Casgevy [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; U.S. Food & Drug Administration. Revised December 2023. Accessed September 17, 2025. https://www.fda.gov/media/174615/download
20. CASGEVY® Brochure | CASGEVY® (exagamglogene autotemcel). Vertex Pharmaceuticals, Inc. 2025. Accessed September 21, 2025. https://www.casgevy.com/sickle-cell-disease/sites/default/files/casgevy_brochure_SCD.pdf
21. Johnson KM, Jiao B, Ramsey SD, Bender MA, Devine B, Basu A. Lifetime Medical Costs Attributable to Sickle Cell Disease among Nonelderly Individuals with Commercial Insurance. *Blood Advances*. 2022;7(3). doi:https://doi.org/10.1182/bloodadvances.2021006281
22. Frangoul H, Locatelli F, Sharma A, et al. Exagamglogene Autotemcel for Severe Sickle Cell Disease. *N Engl J Med*. 2024;390(18):1649-1662. doi:10.1056/NEJMoa2309676

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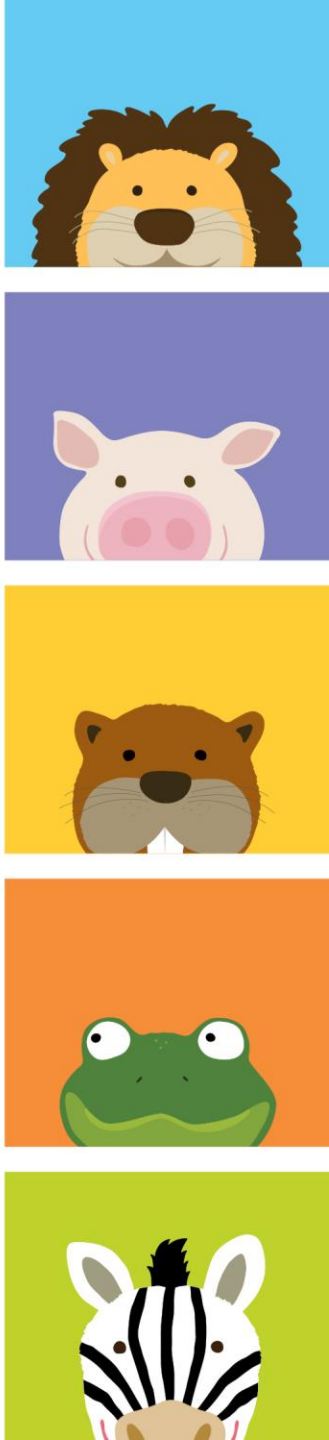

Questions?

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Get Up to Speed with Gene Therapy: Pediatric Pharmacy Implications

Current and Upcoming Gene Therapies in the Pediatric Population

11/11/2025 | Celina Hung, PGY1 Pharmacy Resident, Advocate Christ Medical Center

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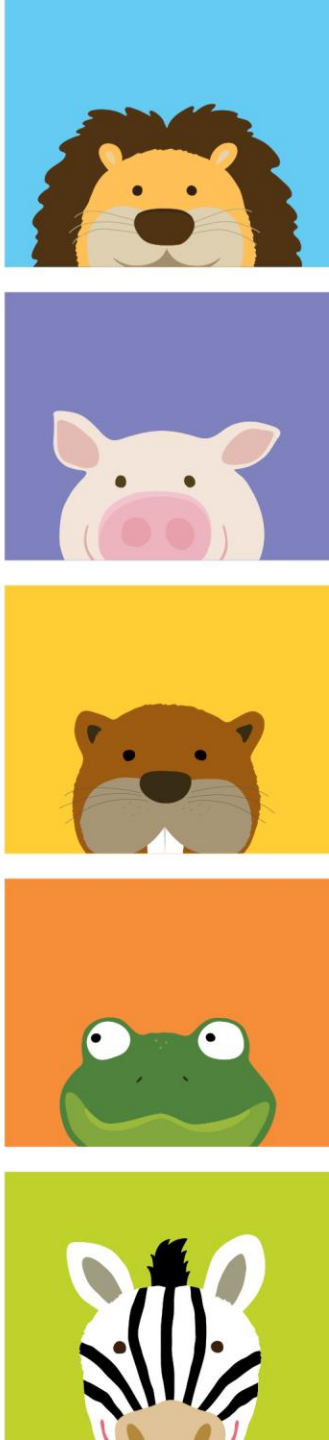
Amendments

Updates to the presentation include the following:

- Slide 10: In addition to the gene and cell therapies mentioned live, it was reported that Kymriah is on formulary and is being used in the pediatric population within the Southeast region for relapsed or refractory B-cell precursor ALL.
- Slide 36: In addition to management strategies listed, risdiplam is an oral treatment used in pediatrics for SMA. Nusinersen (SPINRAZA) is another gene therapy used in pediatric patients.
- Slide 62: Voxelotor was pulled off market; however, if it were to still have been available, it would follow the same timeline of discontinuation as hydroxyurea and crizanlizumab.
- Slide 66: CASGEVY is stored in the stem cell lab. Therefore, stem cell lab technicians are responsible for the storage and handling of exagamglogene autotemcel.



Frangoul H, et al. *N Engl J Med*. 2024;390(18):1649-1662.