

Accelerating access to gene therapy:

Lessons from commercial implementation in sickle cell disease and transfusion-dependent thalassemia

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OBJECTIVE

To characterize a national ecosystem spanning Qualified Treatment Centers (QTCs), specialty labs, centralized manufacturing, and product operations to quantify real-world implementation timelines, uptake, and drivers in routine practice.

CONCLUSIONS

- Recent data collected from patients prescribed beti-cel & lovo-cel is the first to analyze commercial stem cell gene therapy implementation in the U.S.
- Data demonstrates the growing demand for and scalability of one-time gene therapies for sickle cell disease and thalassemia with increasing accessibility.
- Experiences learned from the beti-cel launch and the commercial infrastructure that Genetix has built has enabled rapid access to lovo-cel treatment for people with sickle cell disease nationwide.
- Our commercial implementation sets a benchmark for delivery and reinforces the value of durable, one-time gene therapy for patients, providers, & payers.

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- Kanter J, Walters MC, Krishnamurti L, et al. Biologic and clinical efficacy of lentiviral hematopoietic stem cell gene therapy for sickle cell disease. *N Engl J Med*. 2022;386(7):617-628.

DISCLOSURES

VKP, MAK, BN, TC, KC, RS, TK, JL, and AC: Current employees of Genetix Biotherapeutics. BR: Current employees of Genetix Biotherapeutics and ended employment with Beam Therapeutics in the past 24 months. JL: Current employees of Genetix Biotherapeutics and ended employment with NIKang Therapeutics in the past 24 months.

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INTRODUCTION

Zyntego

Betibeglogene Autotemcel (beti-cel)^{1,2}

- Indication:** ZYNTGLO is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of adult & pediatric patients with β -thalassaemia who require regular red blood cell (RBC) transfusions
- FDA approval:** August 2022
- Mechanism:** ex vivo Gene Addition; Adds functional β A-T87Q-globin gene designed to correct the β / α -globin imbalance in erythroid cells and increase adult Hb
- Dosing:** One-time autologous stem cell transplant

Lyfgenia

Lovotibeglogene Autotemcel (lovo-cel)^{3,4}

- Indication:** LYFGENIA is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events
- FDA approval:** December 2023
- Mechanism:** ex vivo Gene Addition; Adds anti-sickling β A-T87Q-globin gene designed to inhibit polymerization of HbS thereby limiting the sickling of red blood cells
- Dosing:** One-time autologous stem cell transplant

RESULTS

The most robust long-term dataset in ex vivo gene therapy for hemoglobinopathies

- Primary analyses in this poster focus on our experience using recent operational data from patients prescribed Zyntego & Lyfgenia since FDA approval.
- However, our extensive experience across clinical trials and commercial patients has provided context to refine and optimize the patient journey.
- Overall, we have treated 138 patients with up to 11.2 years of follow up in clinical trials. Between the two products we have over 900 patient years experience.

Table 1. Clinical and Commercial Experience: Patients Treated and Follow-Up

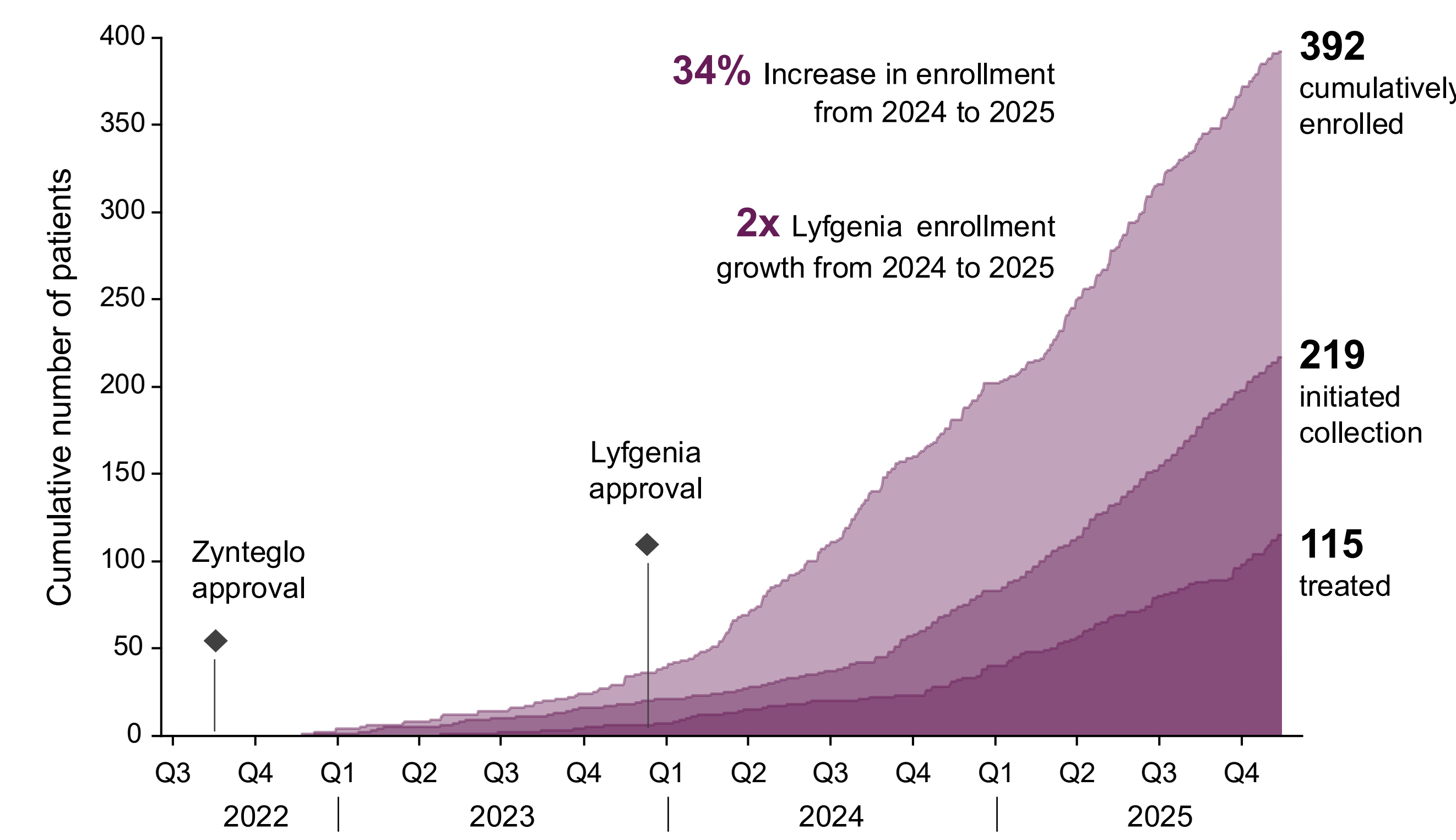
	Patients Treated	Longest Follow-up (Years)	Patient Years
Clinical trials beti-cel	63	11.2	562
Commercial Zyntego	78	2.6	
Clinical trials lovo-cel	75	10.4	369
Commercial Lyfgenia	37	1.2	

lovo-cel clinical data cut as of July 30, 2025; beti-cel clinical data cut as of November 29, 2025; Commercial Lyfgenia and Zyntego data extract as of November 14, 2025

Consistent Growth in Patients Advancing Through Treatment Pathway

- Kinetics of real world activity across programs since the first product approval demonstrates increasing momentum.
- Early phases following approval of Zyntego, focused on onboarding and activating QTCs, and pioneering with partners to navigate processes, across enrollment, collection and treatment.
- There is a continued increase in the steepness of the curve post Lyfgenia approval in 2023.

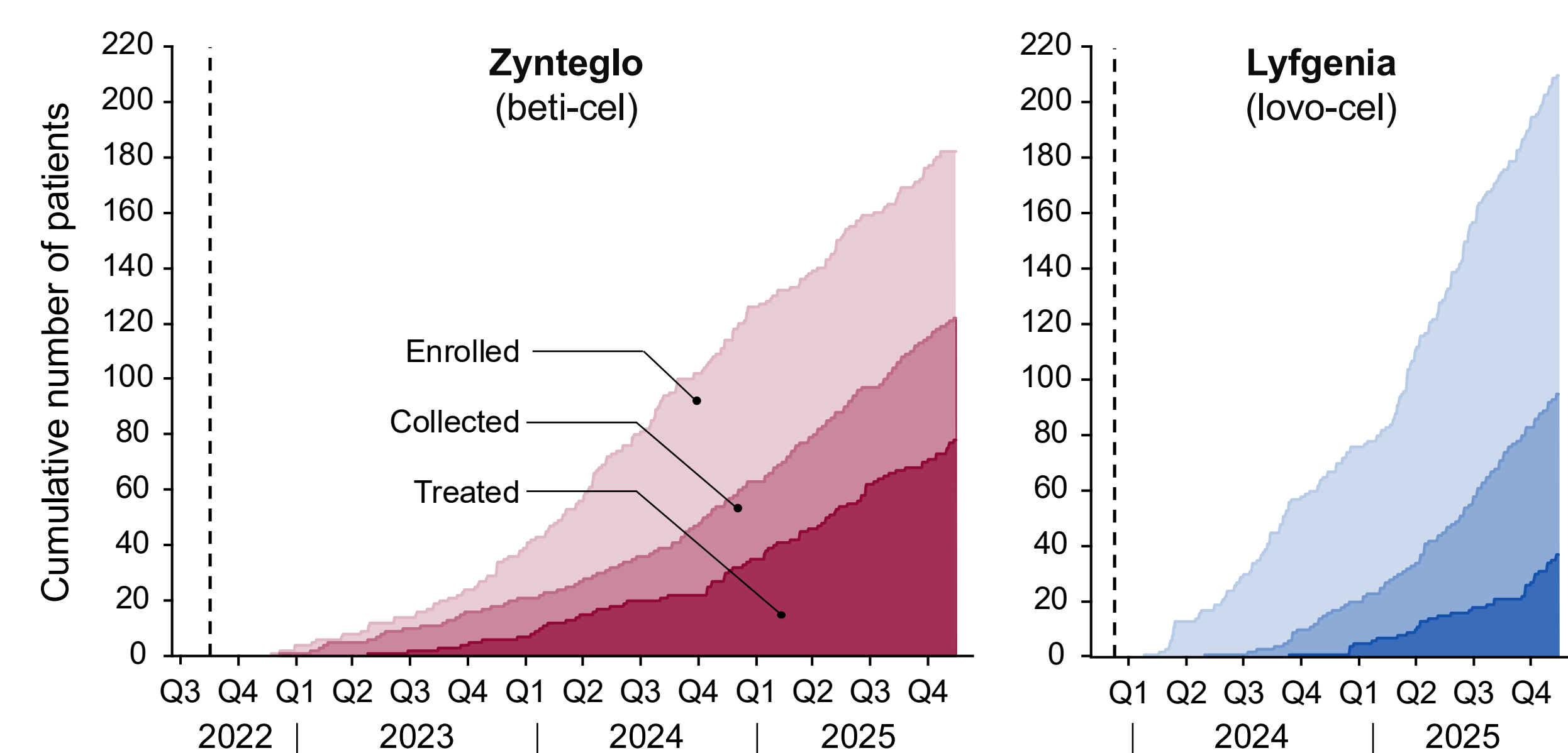
Figure 2. Cumulative Growth in Patient Enrollment, Collection, and Treatment Over Time



Experience from Zyntego launch supported rapid uptake of Lyfgenia

- Compared to Zyntego, Lyfgenia timing from approval to first patient enrolment was twice as fast, and first quarter enrolment rates were 167% higher.
- There were 6-fold more Quality Treatment Centers (QTCs) activated at the time of Lyfgenia approval.

Figure 3. Cumulative Growth Over Time Per Commercial Product



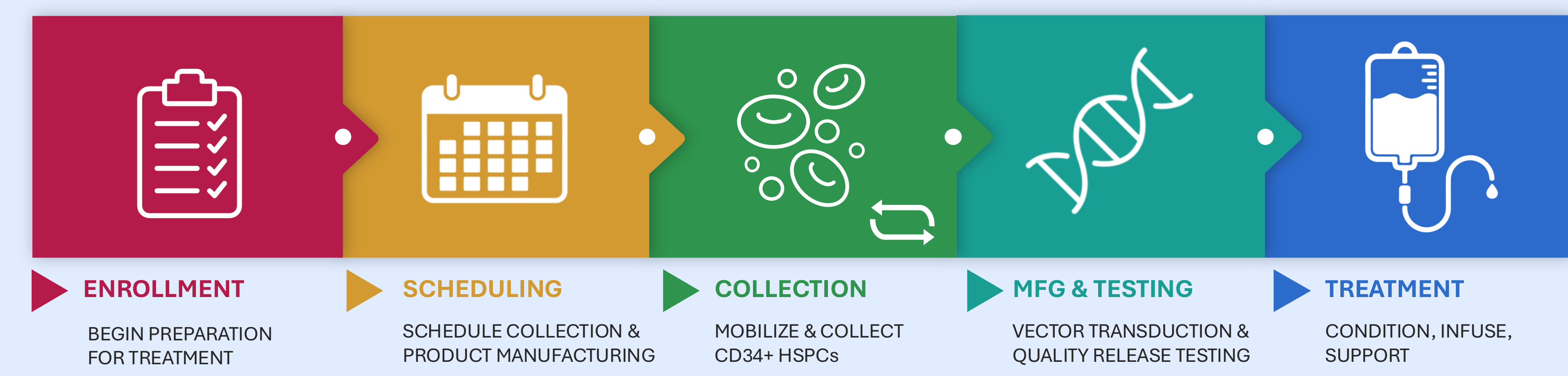
METHODS

The patient journey consists of 5 key steps:

- Enrollment:** QTCs ready patients for therapy medically and financially and submit enrollment to Genetix
- Scheduling:** QTCs schedule patient's cell collection and complete medical preparation of patient
- Collection:** Mobilization and collection of hematopoietic stem/progenitor cells (HSPCs) and shipment to manufacturer
- Manufacturing & Testing:** Drug product is manufactured, meets dose and passes quality release testing before shipment to treatment center
- Treatment:** Patient is admitted for conditioning and infusion of the drug product and is monitored until recovery

All data was collected from operational outputs as of November 14, 2025, unless otherwise specified.

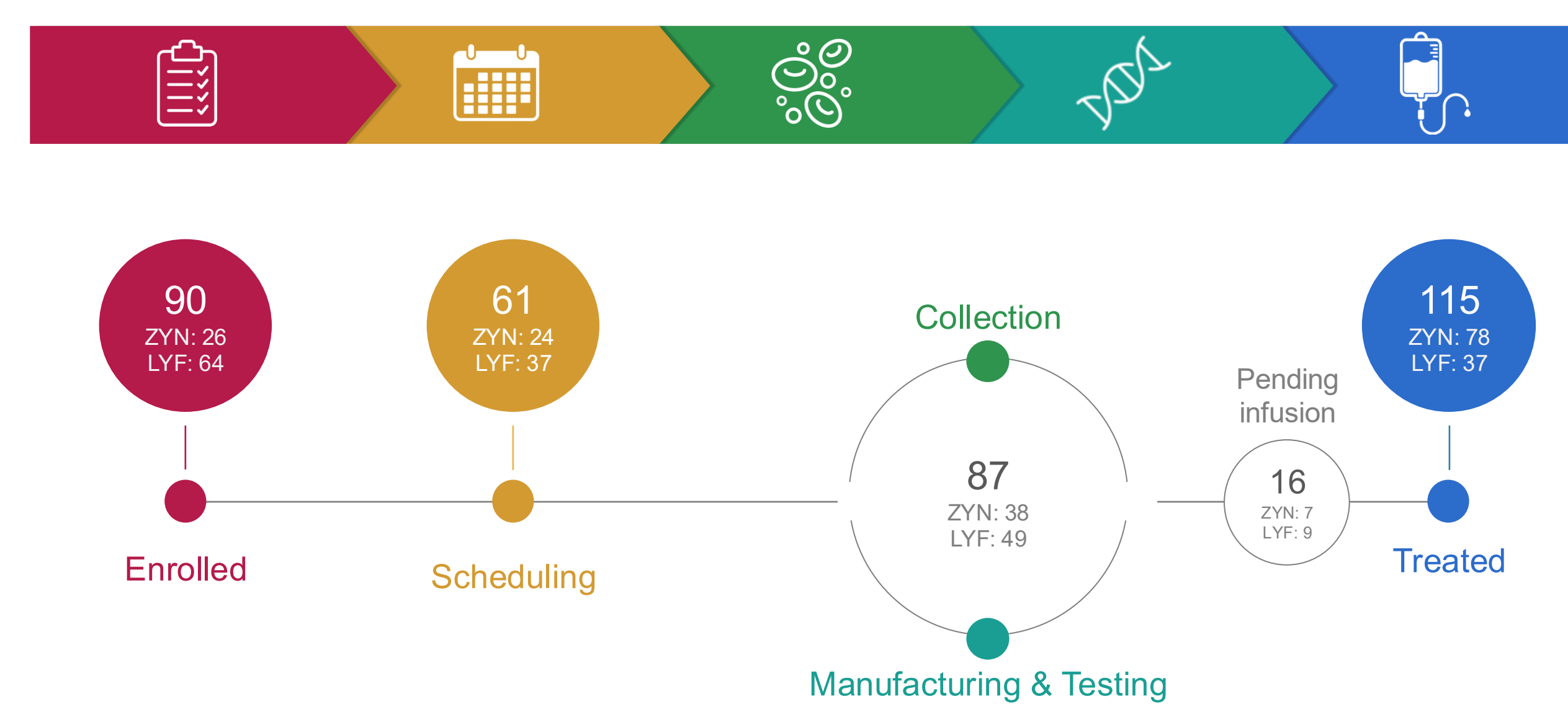
Figure 1. Graphical Depiction of the Treatment Journey



Patients Are Progressing Across All Steps of the Treatment Pathway

- For any given snapshot in time, there are patients at all stages of the pathway
- In addition to 115 treated patients, there were another 254 patients distributed throughout the process.
- This snapshot represents 94.1% of enrolled patients who are currently active in the pipeline or treated*.
- Having patients in every step - and not accumulating in one place - means we are successfully supporting patients through the pathway to treatment.

Figure 4. Snapshot of the patient pipeline as of November 14, 2025



*n = 23 patients cancelled therapy, with 2 patients currently on hold

Real-World Analysis of the Patient Journey identifies Key Drivers

Critical steps that impact the treatment timeline are opportunities to streamline the patient and provider experience:

- Enrollment:** Timing of enrollment may be before or after payer approvals.
- Scheduling:** Scheduling lead times are dependent on manufacturing capacity and increasing demand.
- Cell collection:** If additional cell collection is needed, the patient journey timeline is extended by ~82-days*.
- Manufacturing & Testing:** The largest share of the overall timeline includes comprehensive quality testing.

Table 2. Enrollment-to-Treatment Lead Time

	Zyntego (beti-cel)	Lyfgenia (lovo-cel)
Median time to treatment, months	9.9	8.0
Treated within 12-mos of enrollment (percent)	72	76

Figure 5. Patient Journey Timelines for Zyntego and Lyfgenia by Treatment Step

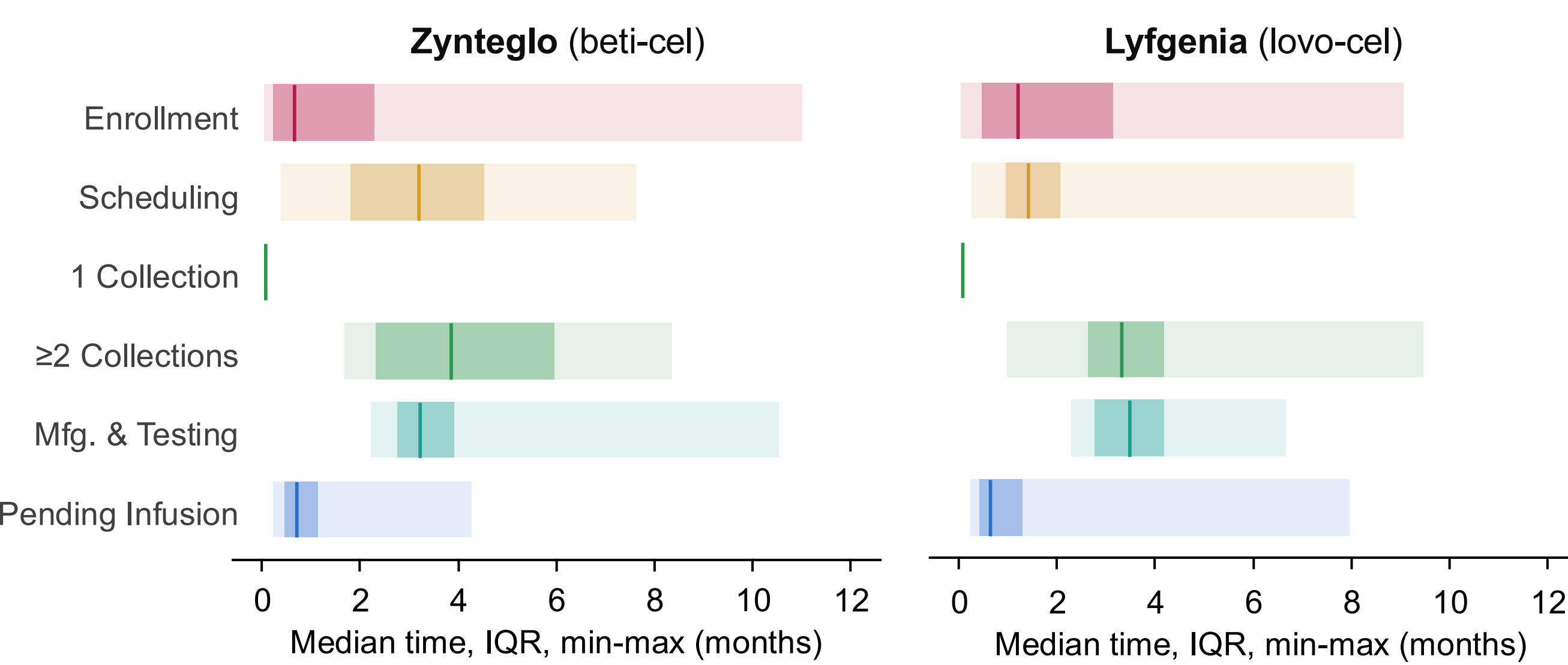


Table 3. Median Time per Treatment Stage for Zyntego and Lyfgenia

Treatment Stage	Zyntego (beti-cel) median time, months	Lyfgenia (lovo-cel), median time, months
Enrollment	0.7	1.2
Scheduling	3.2	1.4
1 Collection	2 days	2 days
≥2 Collections	3.8	3.3
Mfg. & Testing	3.2	3.5
Pending Infusion	0.7	0.6

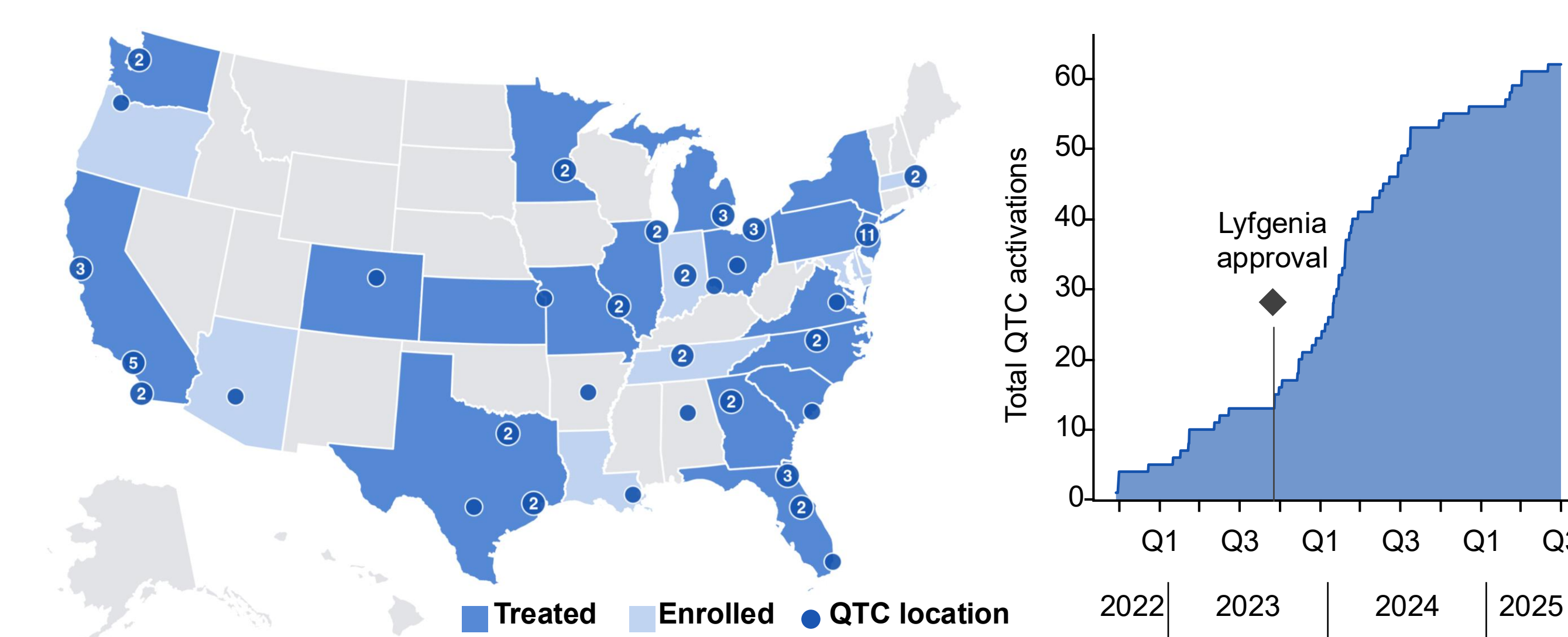
Data for Table 2, Figure 4, and Table 3 n = 115 treated patients; boxplots show median times, with darker shading denoting the interquartile range (IQR), and the range (min, max) denoted by the lighter shading; median times are represented in months unless otherwise denoted; *time per cell collection estimated by linear mixed effects model accounting for product, site, and program maturity

Zyntego & Lyfgenia have the largest network of gene therapy treatment centers for hemoglobinopathies across the U.S.

- We are addressing access and enrollment by broadening the QTC network to 70 activated QTCs nationwide.
- As of November 2025, 115 patients had been treated nationwide, with 39 patients treated in the Northeast, 27 patients treated in Western U.S., 27 patients treated in Southern U.S., and 22 patients treated in the Midwest.
- In addition, we have worked with the Center for Medicare and Medicaid Innovation (CMMI) to establish the Cell & Gene Therapy (CGT) Access Model, which will enable faster Medicaid treatment pathways. The 35 enrolled states represent 84% of U.S. Medicaid SCD beneficiaries.*
- 88% of Lyfgenia QTCs operate in CGT Access Model States.

*Source: CMS CGT Access Model participation list, as of July 15, 2025 (https://www.cms.gov/priorities/innovation/innovation-models/cgt)

Figure 6. Geographic Distribution and Cumulative Activation of Quality Treatment Centers

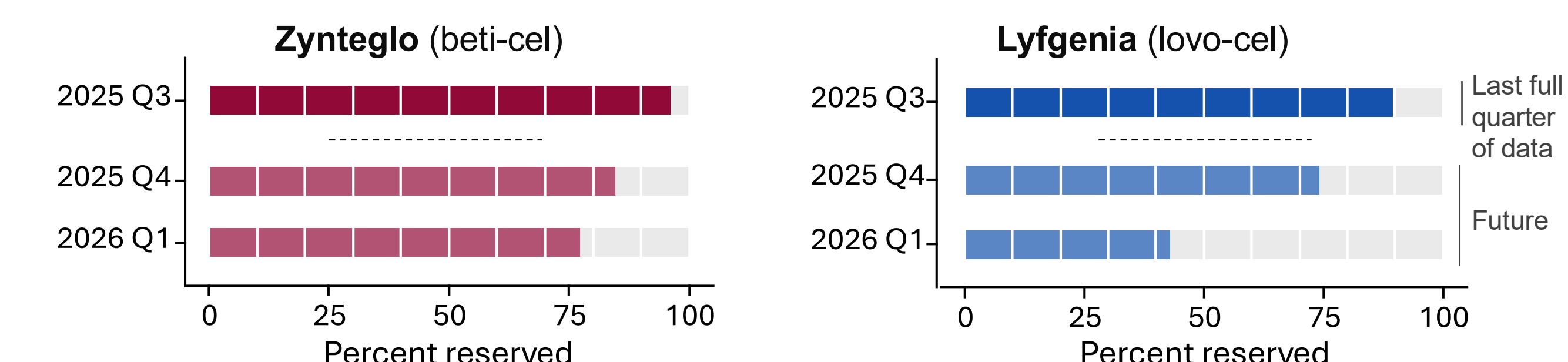


Activation Data as of July 25, 2025 ; number on the QTC location marker denotes the number of QTCs within a 70-mile radius (plotted as a single point at region centroid)

Expanded Manufacturing Capacity Enables Faster Scheduling and Collection Initiation

- Scheduling of collection is directly tied to available manufacturing slots therefore expanding manufacturing capacity would ensure slots are available when patients and providers are ready.
- We are using our current capacity efficiently, however demand is expanding rapidly. To address this need, we are planning on expanding the manufacturing capacity to allow for more timely scheduling of collections.

Figure 7. Percent Reserved Manufacturing Capacity: November 2025 snapshot

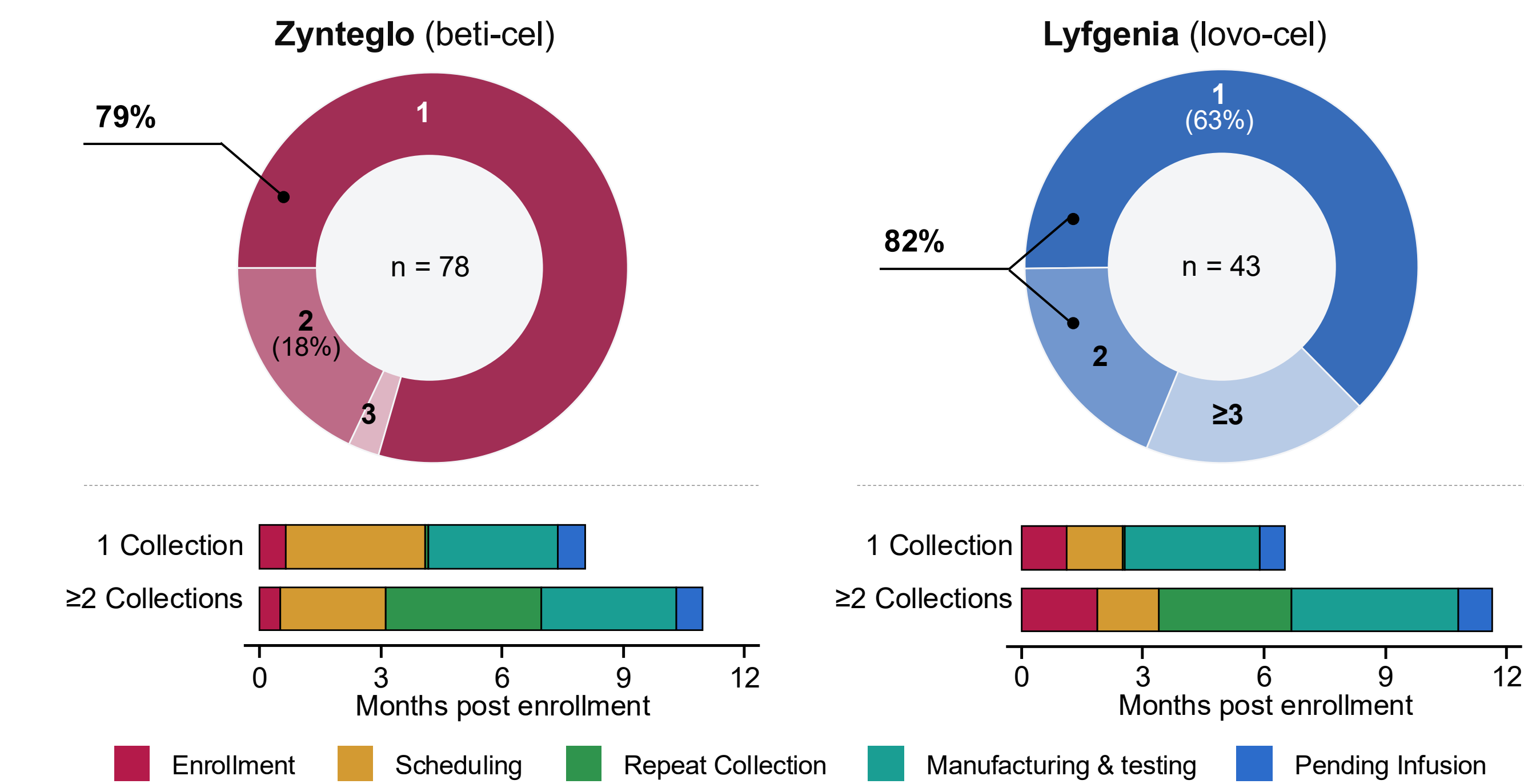


Zyntego data includes capacity for SKYSONA.

Collection Success Enables Timely Progression to Treatment

- Collection success in 1 cycle is a key variable for the overall patient journey timeline.
- The majority of commercially treated patients require 1 cell collection.

Figure 8. Impact of Cell Collection Cycles on Treatment Timelines for Zyntego and Lyfgenia



Collection defined as 2 subsequent days of mobilization and apheresis; collection statistics for Lyfgenia patients include all patients who are ≥6 months after their first collection as of data cut (37 treated); bottom graphs n = 115 treated patients