NEW ENGLAND
REGIONAL NETWORK

NEW ENGLAND REGION
CASE PRESENTATION

January 14, 2026

PRESENTERS

Adrienne Zhan, AGPCNP-BC

- Nurse Practitioner
- Mount Sinai Hemophilia Treatment Center

Nathan T. Connell, MD, MPH, FACP

- Associate Director
- Boston Bleeding Disorder Center

Salley G. Pels, MD

- Medical Director
- Brown University Health Hemostasis and Thrombosis Center

PRESENTERS

Instructions for Credit

1. Visit https://cme.partnersed.com/CCSJan26
2. Complete the activity evaluation
3. Upon completion of all evaluation questions, your credit will be made available for download immediately.

NER Clinical Case Series: Gene therapy administration for severe FIX deficiency

Adrienne Zhan, AGPCNP-BC

Mount Sinai Hemophilia Treatment Center

January 14, 2026

Mount Sinai

HEMGENIX Patient #1

- 56 years old
- Severe FIX, diagnosed at age 7
- History of Hep A/B/C (s/p Harvoni), HIV on HAART
- No history of inhibitor
- Bleed history:
  - GI bleeding (duodenal ulcers)
  - Trauma
  - L arm bleed in 2021
- Rebinyn weekly prophylaxis
  - Tried and failed Alprolix, Idelvion, Benefix
- Fidelis Medicaid

Pre-infusion Workup

- Patient motivated/self-selected for HEMGENIX administration
- AAV5 antibody titer negative
- Baseline AST = 15 U/L, ALT = 14U/L
- HBV and HCV negative for active infection
- HIV viral load undetectable
- Fibroscan
  - Fibrosis F0-1
  - Steatosis S0
- Liver ultrasound
  - Mildly echogenic liver, compatible with nonspecific parenchymal disease, including but not limited to hepatic steatosis

Infusion Day 10/9/2024

- 08:00 arrival time
- Mild URI symptoms
- 2 PIVs placed
- Premedicated with diphenhydramine 25mg PO
- Infusion started 09:50, finished 10:50
- No infusion reaction
- Discharged home at 13:52

Post-Infusion Monitoring

- Factor IX: 39-41%
- AST max: 21 U/L 3/26/25 (24 weeks)
- ALT max 20 U/L 3/26/25
- Cut finger 11/27/25, infused Rebinyn x 1 (FIX ~30%)
- 1 year visit 10/24/25
  - AFP < 2
  - Abdominal ultrasound unremarkable

New England Region Hemophilia Network:
Clinical Case Series

Hemophilia Gene Therapy Clinical Case: A 29-year-old man with severe hemophilia B

Nathan T. Connell, MD, MPH, FACP

Associate Director, Boston Bleeding Disorders Center
Vice Chair of Medicine, Mass General Brigham
Associate Professor of Medicine, Harvard Medical School

BOSTON BLEEDING DISORDERS CENTER

Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Disclosures

Disclosures	
Director, Officer, Employee	Brigham and Women's Hospital
Shareholder	Doximity
Honoraria	OctaPharma AG and Roche
Advisory Committee	Bayer, CSL Behring, Genentech, Medzown, Pfizer, Sanofi Genzyme, SeraGene, and Takeda
Consultant	OctaPharma AG and Takeda

Case Presentation

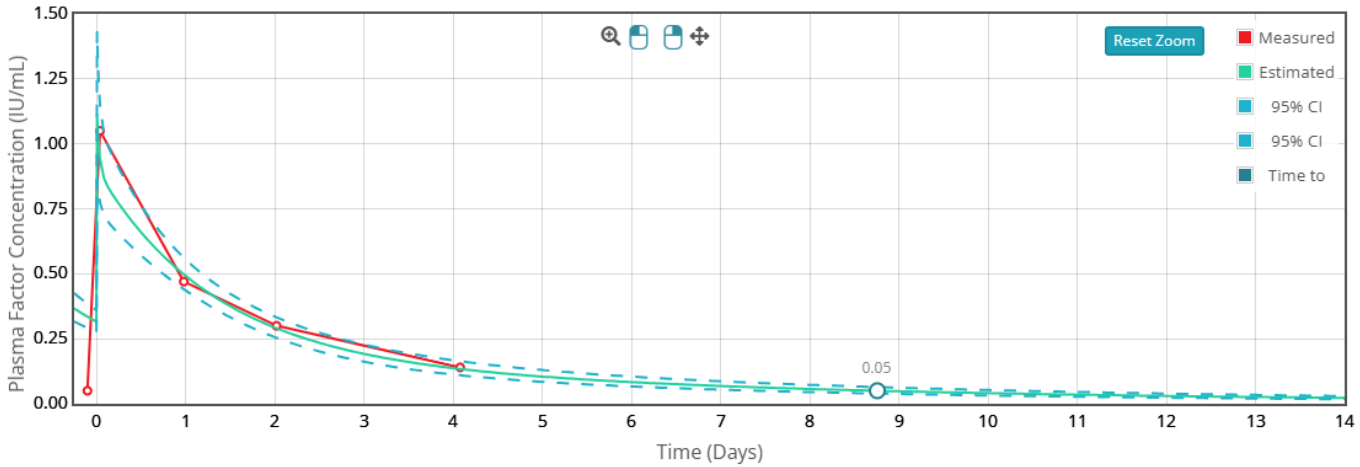
- 26-year-old man, originally from Belarus, who presented to establish care for hemophilia B
- Diagnosed with severe hemophilia B at 9 months of age after lingual frenotomy
- Treated with on-demand approach with plasma-derived FIX
- Target joint: Right ankle (Every 1-2 weeks to now monthly)
- History of life-threatening neck bleed compromising airway

Case Presentation: Initial Priorities

- Laboratory testing to evaluate for an inhibitor
- Initiate FIX prophylaxis
- Orient him to the hemophilia treatment center resources
- Aggressive physical therapy regimen
- Teach him to self-infuse

Case Presentation: Clinical Stabilization

- Significant improvement in right ankle/overall functional status
- Converted to EHL FIX (eftrenonacog alfa; FIX-Fc) with PK studies
- He expressed interest in hemophilia B gene therapy



Estimate (hr)			
Parameter	Conservative	Balanced	Optimistic
Time to 0.05 IU/ml	177.75	210.25	248.5
Time to 0.02 IU/ml	313	356.75	406.5
Time to 0.01 IU/ml	451.75	505.25	565
Half-life	87.75	93.75	100.25

Gene therapy consultation

- Factor IX baseline activity: <1%
- Factor IX inhibitor: No factor inhibitor detected
- AST: 45, ALT 78 (ULN 50), ALP 76, Tbili 0.7, Cr 0.89
- AAV5 NAb: Negative
- Hepatic ultrasound/elastography:
  - Diffusely increased echogenicity consistent with fatty liver. Areas of fatty focal sparing seen.
  - Median estimated Young's modulus is 5.42 kPa (nl 2.5 – 7 kPa)
- Hepatology consult:
  - Most likely metabolic-dysfunction associated steatotic liver disease (MASLD)
  - Weight loss; Mediterranean diet; increased exercise; alcohol avoidance

Etranacogene dezaparvovec

Infused 205 x 10^{13} genome copies

[Weight: 102.5 kg]

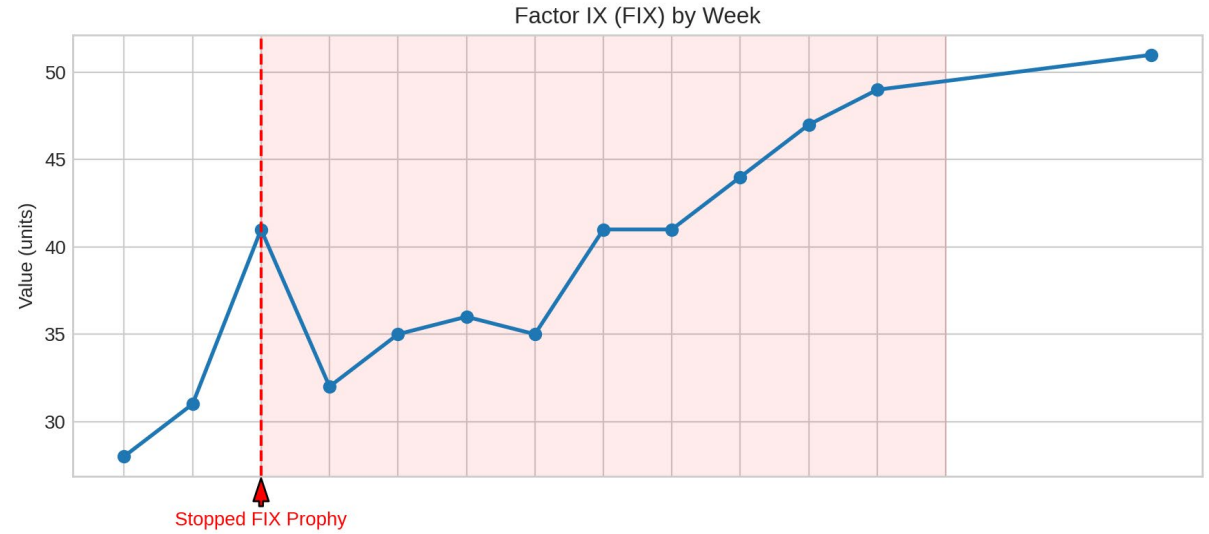
No infusion reactions

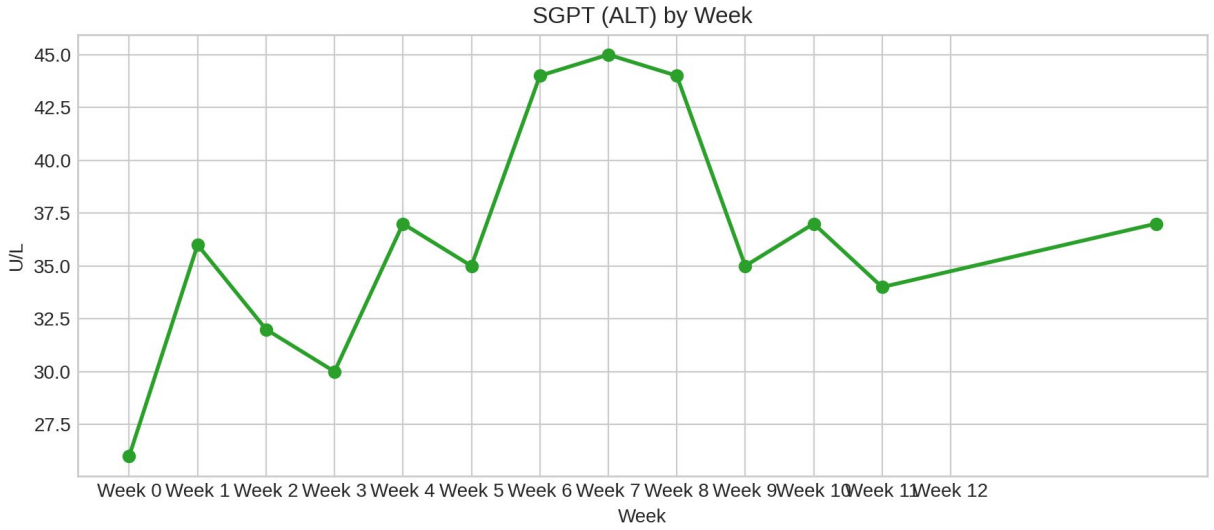
Experienced mild flu-like symptoms over next 24-48 hours

Began lab monitoring phase

Post-infusion monitoring

- Weekly LFTs and FIX activity
- FIX prophylaxis stopped during week 3 post-infusion
- Slow rise in ALT, but never above ULN or 2x pre-infusion baseline
- No need for corticosteroids
- Peak FIX activity 51%





Case Presentation: Key Takeaways

- 26-year-old man with severe hemophilia B, initiated on FIX prophylaxis, and then successfully treated with etranacogene dezaparvovec gene therapy who has not needed any FIX infusions for > 6 months
- Trust between patient and gene therapy treatment center
- Shared decision making about known efficacy, uncertain duration, risk of returning to prophylaxis, barrier contraception needs, identity within bleeding disorders community
- Significant institutional infrastructure needed to successfully navigate non-clinical aspects of gene therapy infusion

BOSTON BLEEDING DISORDERS CENTER

Brigham and Women's Hospital
Founding Member, Mass General Brigham

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HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Gene Therapy @ Brown

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BROWN Health
UNIVERSITY

Outline

1. Case presentation
2. Patient eligibility
3. Psychosocial factors
4. Institutional readiness
5. Pharmacy Preparedness
6. Timeline Infusion day
7. Post-infusion monitoring
8. Patient Update

Disclosures

None of the presenters have any disclosures

Case Presentation (MV)

- 39-year-old male with Hemophilia B
- Baseline factor IX level <1%
- Prophylactic factor Alprolix 5500 units +/- 10% every 7 days started this regimen 01/2016
- Bleeding symptoms: nosebleeds with season changes, prolonged bleeding from cuts, joint bleeds and target joints (right elbow, right knee, right ankle) – Tylenol and PT as needed – No opioids at home
- HIV negative as of 2024
- Hepatitis C positive at age 18 treated with INF and Ribavarin
- Previous smoker with cigarettes and cigars, previous social alcohol use and history of NAFLD
- Married, 2 children

Gene Therapy Eligibility

(MV)

FDA/PAYER REQUIREMENTS:

Patient clinical characteristics:

- ☑ Male, ≥18 yrs of age
- ☑ A baseline Factor IX activity level of ≤2%
- ☑ Negative Factor IX inhibitor testing
- ☑ History of joint bleeds and target joints (e.g., R ankle, elbow & knee).
- ☑ Patient is currently prescribed prophylactic Factor IX therapy (Alprolix)
- ☑ No prior history of gene therapy
- ☑ No other contraindications

Patient has undergone screening for treatment eligibility, including:

- ☑ Evaluation of liver function (hepatic function panel and liver elastography, clearance by hepatologist)
- ☑ FIX Inhibitor testing

ADDITIONAL CONSIDERATIONS PER HTC SOP:

- ☑ Neutralizing antibody titer (Nab) (titer =65)
- ☑ Patient has been seen and evaluated by our HTC providers
- ☑ Patient able to adhere to follow up and lifestyle recommendations
- ☑ Patient will have an adult ≥18 yrs of age present with them throughout the infusion visit and for 24 hrs after discharge
- ☑ Insurance authorization obtained

Psychosocial Factors

(GC)

- Clinical Social Work Role
- Address psychosocial needs i.e. biopsychosocial assessment
- Ongoing emotional support
- Review informed decisions
- Explore financial costs
- Assist family members through this life changing experience
- Monitor patient's coping ability with follow up care i.e. lab work, potential side affects/symptoms
- Provide any necessary resources for managing stress

Psychosocial Factors

(GC)

- What are the psychosocial issues to be expected if I undergo gene therapy?
- You may have conflicting feelings after you undergo gene therapy or any other major life change. Examples could include guilt, feeling of not belonging to the community or fear of how the therapy might impact you in the future. This is completely normal. It is important that you speak with your HTC or primary care provider who can help you understand these feelings. Your HTC may also be able to put you in touch with another patient who is also enrolled in a gene therapy trial.

GT Institutional Readiness (SP)

HTC

- HTC 340B program → **DSH**
- Infusion location → Pedi Clinic
- HTC SOP*
- Training & Education

INSTITUTIONAL

- High-Cost Drug Committee
  - HTC/SME
  - Pharmacy Leadership
  - Contracting
  - Legal
  - Marketing
- P&T Committee
- ITS Epic build

PAYER CONTRACTING

- Legal & contracting, single case agreement
- Prior authorization

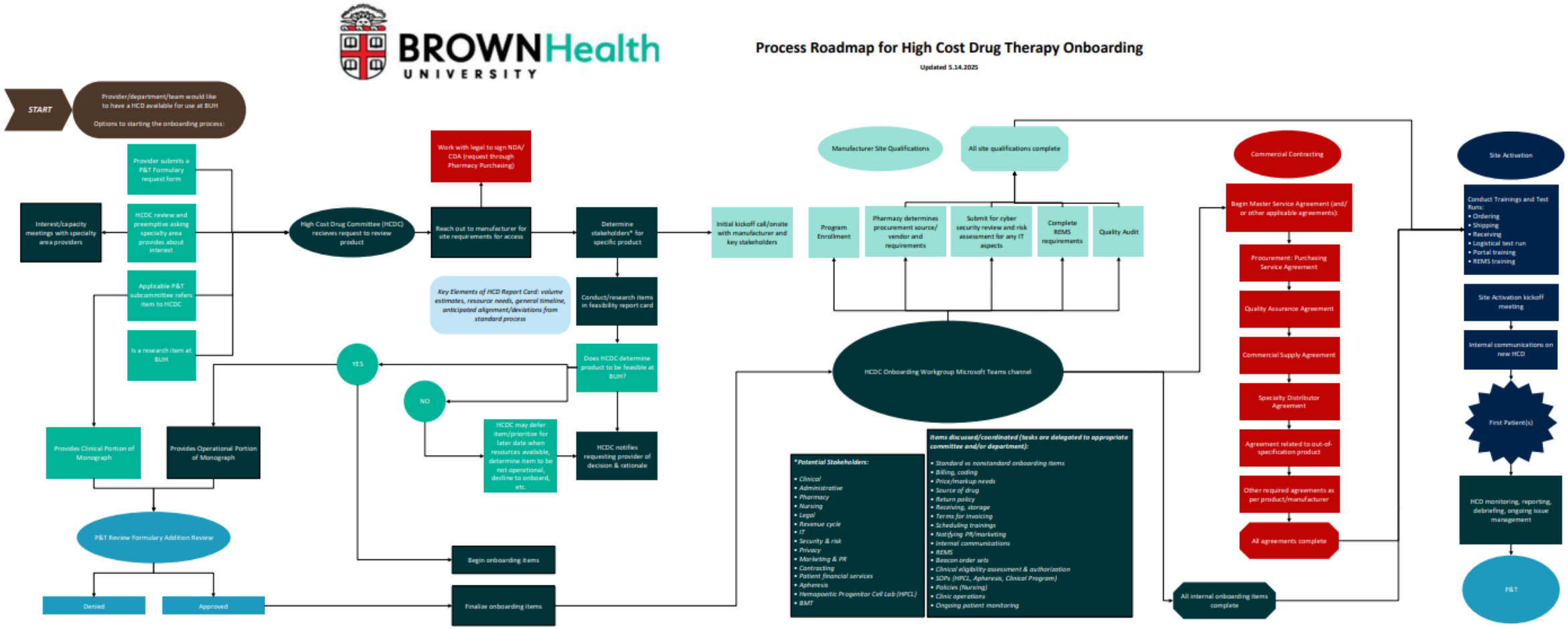
PHARMA (CSL)

- Legal & contracting, purchase agreement and rebates
- CSL liaison (Andrew Paley)
- Prior auth assistance
- Hemgenix connect program
- Hemgenix administration center (in-service training completed)

High-Cost Drug Therapy Process Roadmap

(SP)

*Modified from UCDavis



High-Cost Drug Therapy Process Roadmap

(SP)

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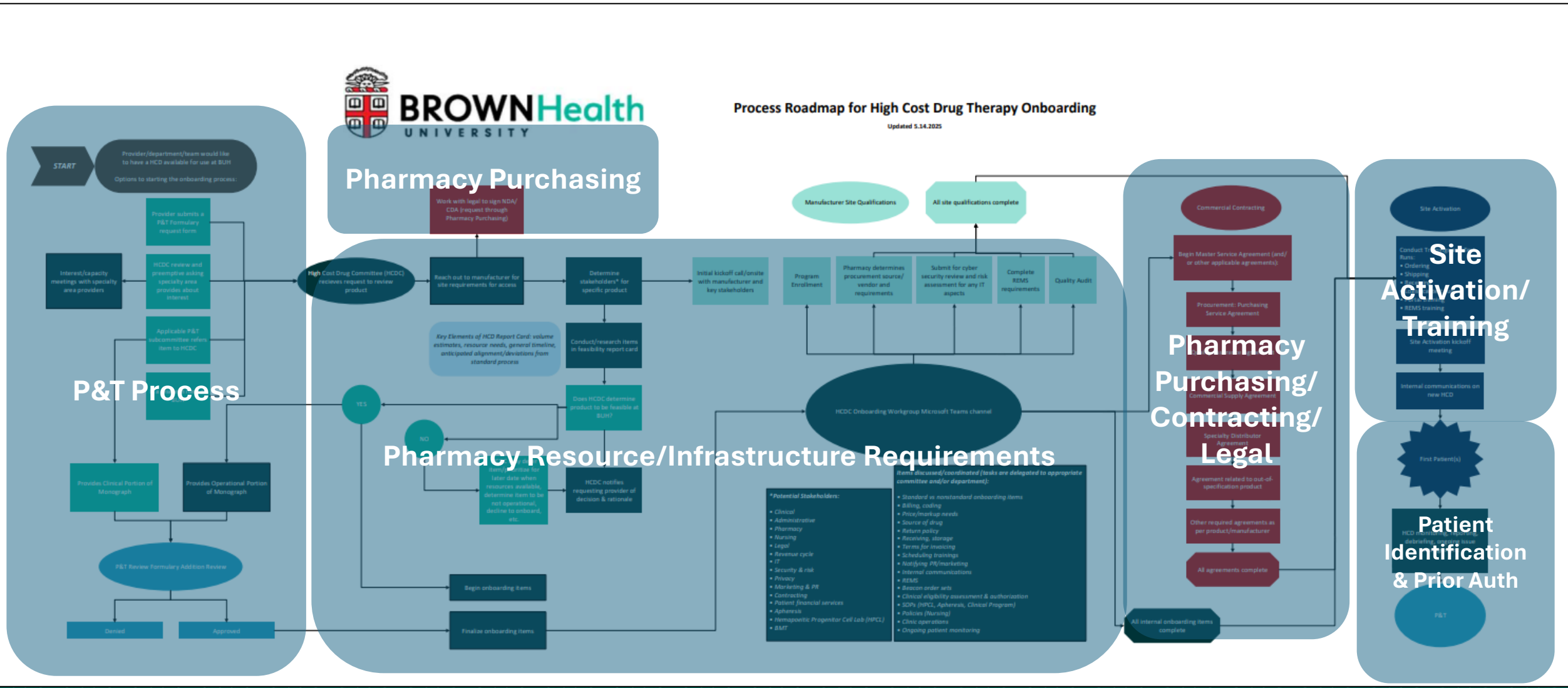
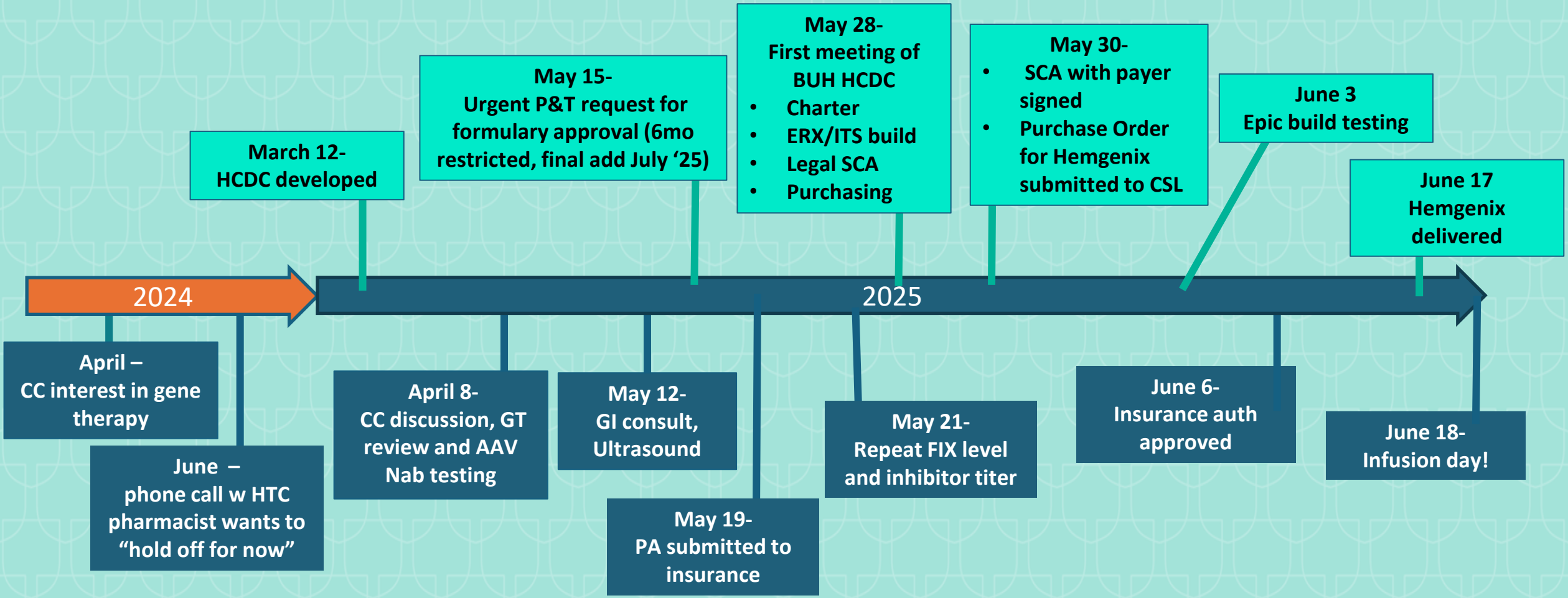


Timeline

(SP)


2024
2025
April –
CC interest in gene therapy
June –
phone call w HTC pharmacist wants to "hold off for now"
March 12-
HCDC developed
April 8-
CC discussion, GT review and AAV Nab testing
May 15-
Urgent P&T request for formulary approval (6mo restricted, final add July '25)
May 12-
GI consult, Ultrasound
May 19-
PA submitted to insurance
May 28-
First meeting of BUH HCDC
Charter
ERX/ITS build
Legal SCA
Purchasing
May 21-
Repeat FIX level and inhibitor titer
May 30-
SCA with payer signed
Purchase Order for Hemgenix submitted to CSL
June 6-
Insurance auth approved
June 3
Epic build testing
June 17
Hemgenix delivered
June 18-
Infusion day!

Pharmacy Preparedness

(RH)

- Emergent formulary approval request to BUH P&T Committee, resulting in successful time-limited 6-month approval, pending future full panel review
- Staff in-service training from CSL Behring
- Dry run(s), mock prep, and pharmacy team refresher in hospital cancer center pharmacy / hood
- Product build into Epic, with subsequent data entry into the outpatient retail pharmacy system as a prescription, allowing for order verification by a pharmacist

Pharmacy Preparedness: Day-Of Plan of Action (RH)

- Product shipment by a dedicated delivery service from the manufacturer to the retail pharmacy at the hospital (day prior to infusion)
- CSL Behring team on-site during entire process as supportive sounding board for any questions
- Steps:
  - Product verification and prescription labeling in retail setting
  - Labeled product delivery to cancer center pharmacy for preparation in hood (22 vials to be drawn up and reconstituted)
  - Final product delivery to infusion suite by pharmacy team

Infusion Day (CL)

Time	Details
0815	**Patient arrived** to clinic with mom for Hemgenix infusion. Two #22g PIVs placed, labs drawn. HTC team, marketing and local news crew on site.
0830	Hemgenix medication released by RN. Hypersensitivity med box at bedside. Patient w pre-infusion tachycardia and diaphoresis associated with anticipatory anxiety, managed with support from team (ie CBT techniques, deep breathing, cold compress), no pharmacologic intervention required.
0855	Hemgenix preparation started (per pharmacy recordings)
1045	Hemgenix infusion arrive from pharmacy tech, hand-delivered, checked by 2 RNs
1100	**Hemgenix infusion started** at 500 mL/hr over 60 minutes, no pre-meds
1115	Patient comfortable with VSS
1205	**Infusion complete** without s/s of reaction. Received 100 mL NS at 500 mL/hr to flush remainder of medication through line.
1225	PIV flushed, locked and disconnected. Monitoring started for post-infusion reaction(s)
1300	VSS. Left PIV removed
1400	VSS
1500	VSS. Right PIV removed. No hypersensitivity meds utilized. Patient verbalized feeling tired from the day and was **discharged home** without need for further observation.

**Permission given*

Post-infusion Monitoring

(CL)

- Factor IX activity:
  - weekly (months 1-3)
  - monthly (months 4-12)
  - every 3 months (13-24 months)
  - every 6 months (24+)
- Factor IX inhibitor testing:
  - *monthly for first 3 months, then prn*
- *Liver enzymes*
  - weekly (months 1-2)
  - monthly (months 4-12)
  - every 3 months (13-24 months)
  - every 6 months (24+)
- AFP and Abdominal US (annual)

Post-infusion Events

(MV)

06/19/25 – Patient feeling "absolutely fine" without any symptoms and out of work for the remainder of the week.

06/25/25 – Patient not feeling well with a cold-feeling, lightheaded, nauseous and the chills. Due for labs today (1 week) post-infusion. He relates symptoms to heat exhaustion from work and felt better in the afternoon. Factor IX level 65%.

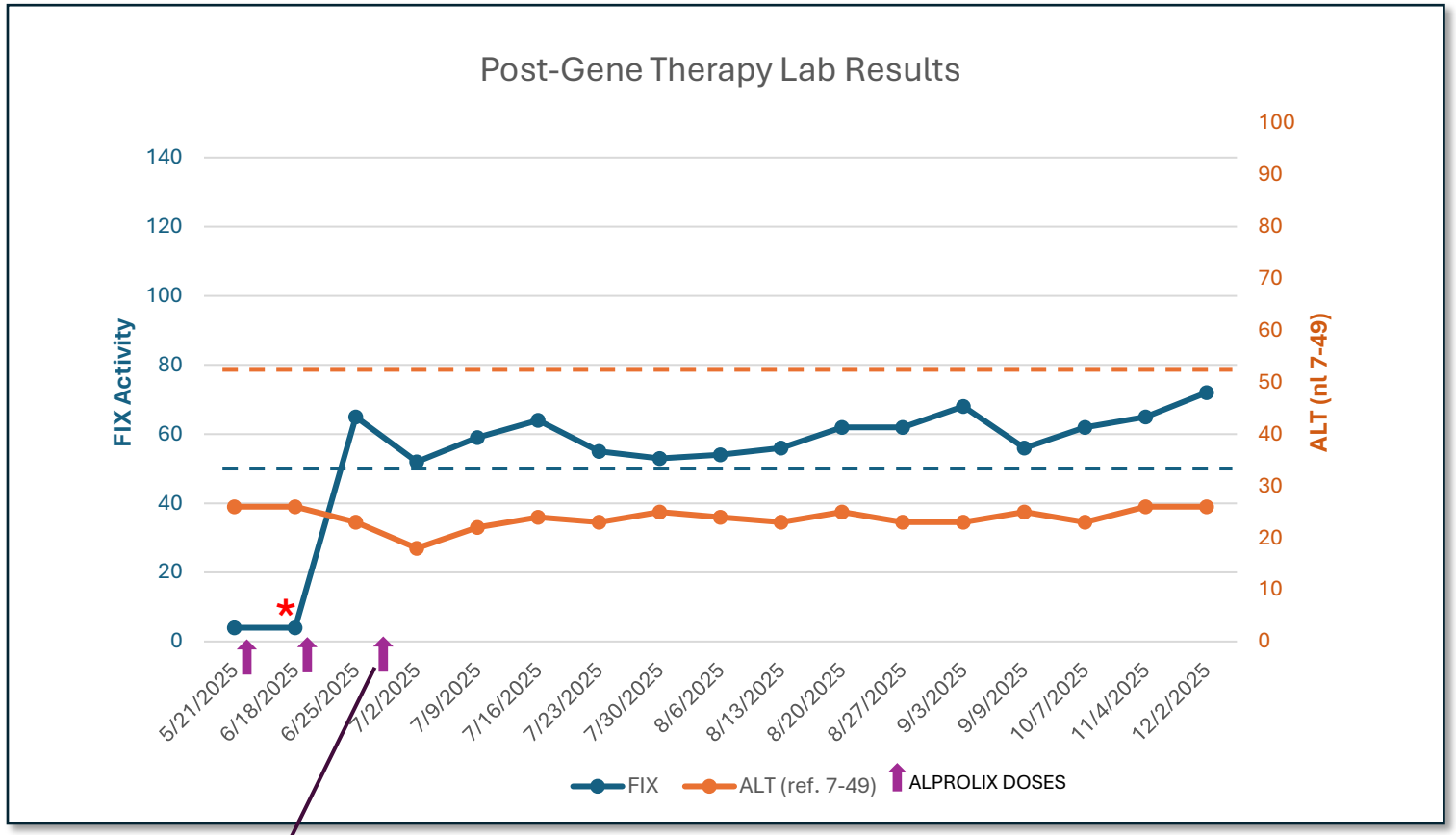
06/29/25 - Administered his last prophy dose of Alprolix since receiving gene therapy. Next lab draw due on 07/02/25.

08/1/25 – C/o right ankle pain, swelling and difficulty walking starting on 07/30 after working. Pain improved with Tylenol. Blood work with FIX level 53% and X-ray revealing osteoarthritis and some joint abnormalities. No factor administered.

Post-infusion Monitoring and Patient Update

- *Hemgenix infusion 6/18/25
- No steroid doses required to date
- Patient is doing well!

(SP)



FIX activity from 6/25 did not result until after 6/29, when patient recieved last infusion

Thank you!

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Questions??