TALPHERA

Corporate overview

Innovative products for medically supervised settings

April 2026

Disclaimers & Forward-looking Statements

Forward-Looking Statements

Some of the information in this presentation is not historical in nature and may constitute forward-looking statements, which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking terminology such as “believes,” “expects,” “anticipates,” “may,” “will,” “should,” “seeks,” “approximately,” “intends,” “plans,” “estimates,” or the negative of these words or other comparable terminology. The discussion of financial trends, strategy, plans or intentions may also include forward-looking statements. These forward-looking statements involve risks and uncertainties that could cause actual results to differ materially from those projected, anticipated or implied by such statements. Although it is not possible to predict or identify all such risks and uncertainties, they may include, but are not limited to, those described in the Company’s annual, quarterly and current reports (i.e., Form 10-K, Form 10-Q and Form 8-K) as filed or furnished with the Securities and Exchange Commission (SEC). You are cautioned not to place undue reliance on any such forward-looking statements, which speak only as of the date such statements were first made. To the degree financial information is included in this presentation, it is in summary form only and must be considered in the context of the full details provided in the Company’s most recent annual, quarterly or current report as filed or furnished with the SEC. The Company’s SEC reports are available at www.talphera.com under the “Investors” tab. Except to the extent required by law, the Company undertakes no obligation to publicly release the result of any revisions to these forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of unanticipated events.

Non-GAAP Financial Measures

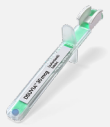
To supplement Talphera’s financial results and guidance presented in accordance with U.S. generally accepted accounting principles (GAAP), the company uses certain non-GAAP financial measures in this presentation, in particular, excluding stock-based compensation expense from its operating expenses. The company believes that this non-GAAP financial measure provides useful supplementary information to, and facilitates additional analysis by, investors and analysts.

TALPHERA

Portfolio overview

Approval

Product	Administration	Phase 1	Phase 2	Phase 3	NDA submitted	Next anticipated milestone
Nafamostat product candidates						
Niyad™	Anticoagulation of the extracorporeal circuit–CRRT/IHD regulated as device					Registrational study expected to be completed in 2026
LTX-608	Various indications regulated as drugs *					
Pre-filled syringe product candidates						
Fedsyra™ 	Ephedrine hydrochloride 10 ml ready to use pre-filled syringe					NDA ready; submission being evaluated
PFS-02 	Phenylephrine hydrochloride 10 ml ready to use pre-filled syringe					NDA submission being evaluated

DSUVIA® (sufentanil) sublingual tablet 30 mcg C-II 

Divested to Alora Pharmaceuticals earning **15%** royalties on commercial sales and **75%** royalties on sales to the Department of Defense, and up to **$116.5M** in milestone payments; Partial monetization of royalty/milestone stream with XOMA Royalty

* Post-toxicology study, expect to be in phase 2 development

TALPHERA

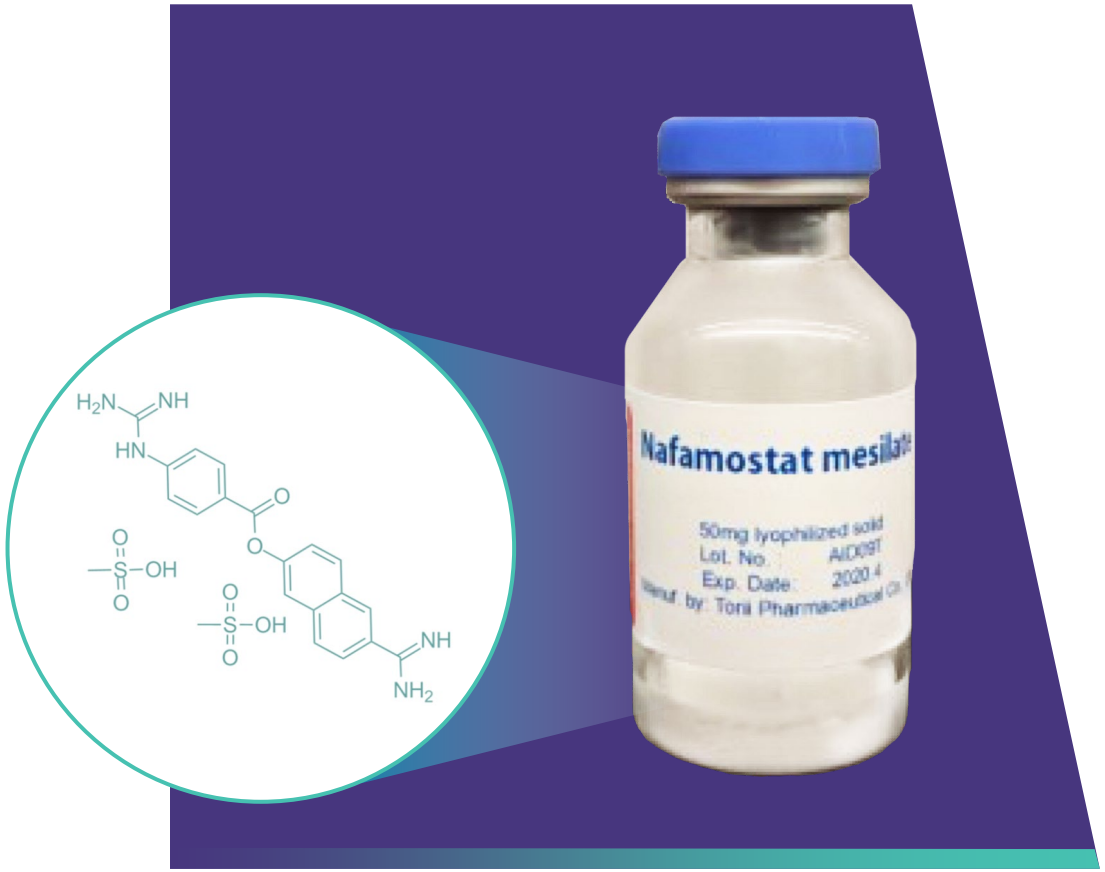
Nafamostat portfolio

Niyad™ and LTX-608

TALPHERA

What is nafamostat?

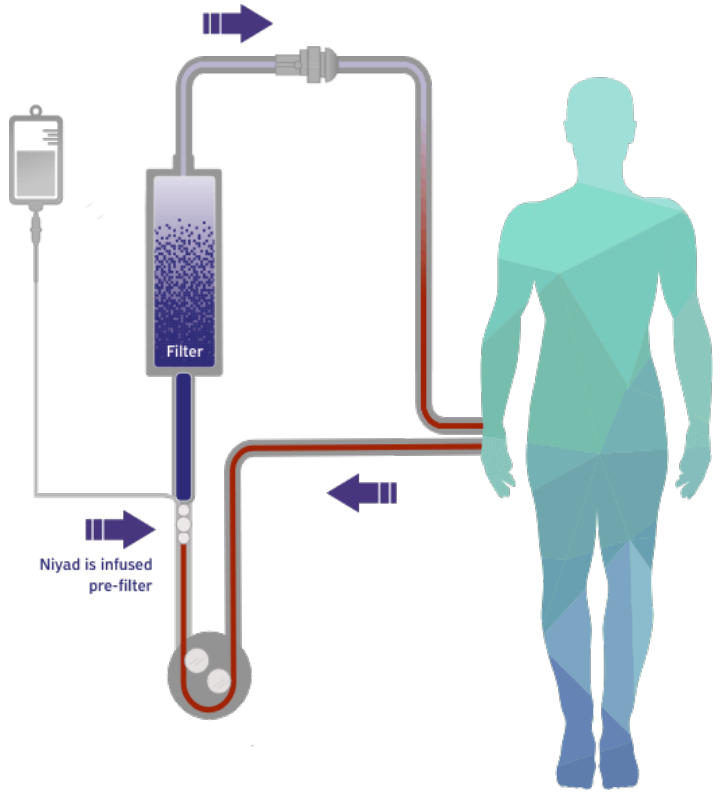
- An investigational broad-spectrum serine protease inhibitor with anticoagulant, anti-inflammatory, mucus clearing and potential anti-viral activities
- Half-life of 8 minutes
- Multiple potential indications given its proposed mechanism of action
- Approved and used in Japan and South Korea for over 30 years
  - Anticoagulation of the extracorporeal circuit
  - Disseminated intravascular coagulation (DIC)
  - Acute pancreatitis
- Various studies performed outside the U.S. for COVID, Acute Respiratory Distress Syndrome (ARDS), Dengue fever and numerous other diseases



Niyad™ is our lead nafamostat product candidate

Talphera is evaluating nafamostat as an anticoagulant for the extracorporeal circuit (blood path outside patient)

- ✓ Niyad has numerous potential **benefits** compared to the standard of care
- ✓ There are **no FDA-approved** regional anti-coagulants for the extracorporeal circuit
- ✓ Niyad is being regulated as a device (works in the circuit)
  - Granted **FDA Breakthrough Device Designation** status for use as a regional anticoagulant in patients receiving CRRT that cannot tolerate heparin or are at a higher risk of bleeding, providing regulatory and developmental benefits
- ✓ **Single registrational study** with endpoints agreed with the FDA expected to be completed in 2026
- ✓ ICD-10 CMS procedural code already received to support **reimbursement**
- ✓ Niyad peak sales for CRRT and IHD estimated at more than **$200 million**



TALPHERA

Exposure of blood to the dialysis filter causes clotting

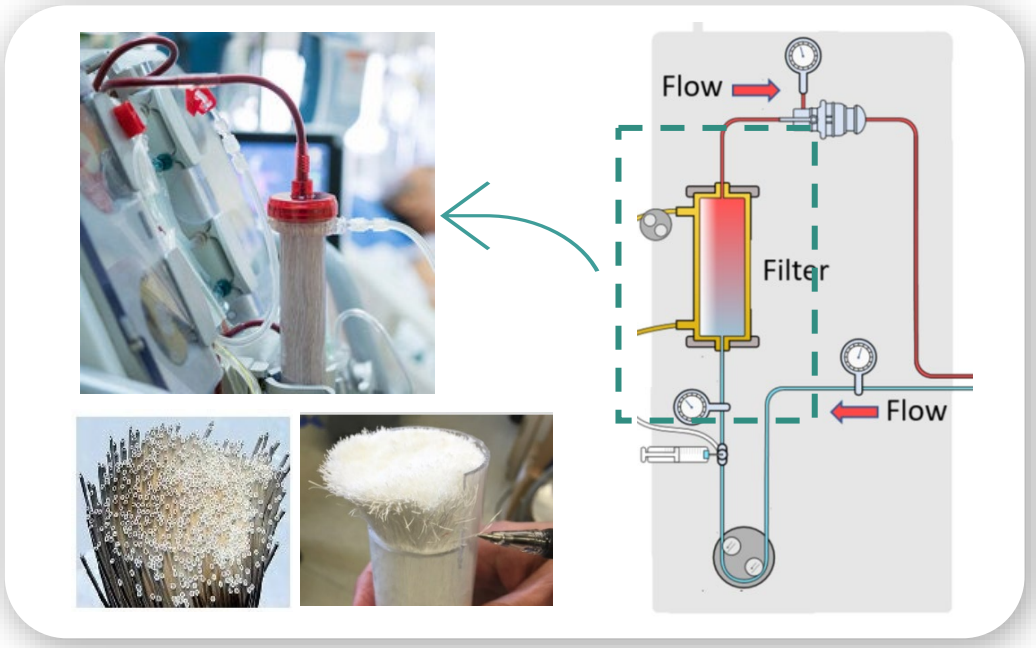
Clotting of the dialysis filter during CRRT is a major limitation to care, as it leads to inefficient dialysis, causes blood loss, and depletes limited resources[1]. Circuit clotting is the most frequent cause of therapy interruption circuit dialysis[2]

More frequent filter changes required to ensure efficacy

Increased blood loss; increased platelet transfusions

Delayed/ prolonged treatment time

Burden on healthcare professional



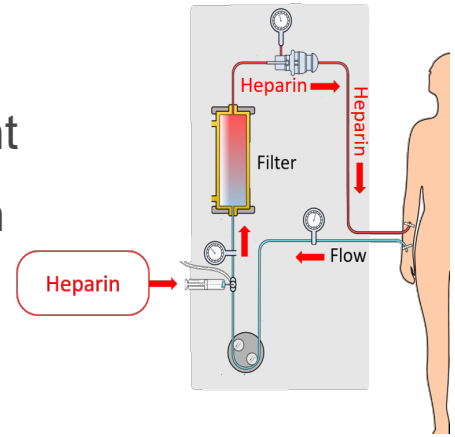
1. Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R. Continuous is not continuous: the incidence and impact of circuit “down-time” on uraemic control during continuous veno-venous haemofiltration. Intensive Care Med. 2003;29:575–578. Zhang Z, Ni H, Lu B. Variables associated with circuit life span in critically ill patients undergoing continuous renal replacement therapy: a prospective observational study. ASAIO J. 2012;58:46–50
2. 2. Clinical review: Patency of the circuit in continuous renal replacement therapy.Joannidis M, Oudemans-van Straaten HMCrit Care. 2007; 11(4):218.

TALPHERA

Current standards for anticoagulation have many disadvantages

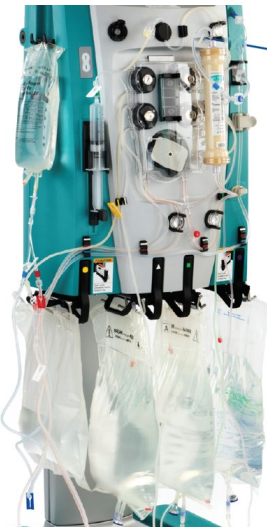
Heparin

- Systemic anticoagulant
- Prolonged half-life up to 3 hours makes it difficult to titrate
- Clinicians fear over anticoagulating the patient
- Significant safety concern for patients at risk of bleeding
- Thrombocytopenia



Citrate

- Citrate chelates calcium, which inhibits the generation of thrombin
- Using citrate requires infusing calcium on the return side of filter (back to patient)
- Extensive, complicated protocol
- Frequent blood draws to measure calcium are time-consuming and expensive
- Rapid changes in calcium levels which can cause hypotension, ventricular fibrillation, and possibly cardiac arrest.
- Even more complicated in patients with liver failure



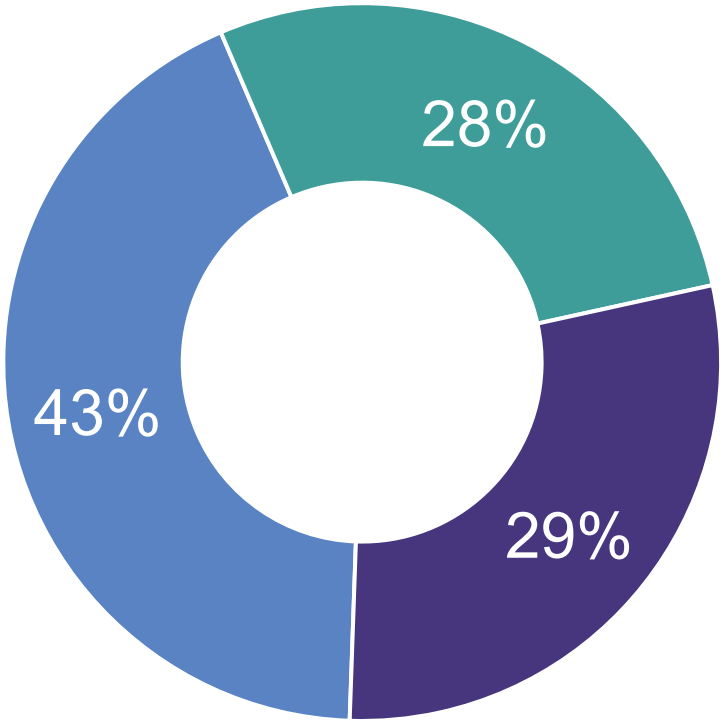
1) Ohtake Y. Nafamostat as Anticoagulant in Continuous HD. Contrib Nephrol. 1991;93;215-217.

TALPHERA

The current market landscape for anticoagulants used during continuous renal replacement therapy (CRRT)

Anticoagulants used in CRRT

Heparin – 43%
(systemic anticoagulant – anticoagulation of the patient and the circuit)



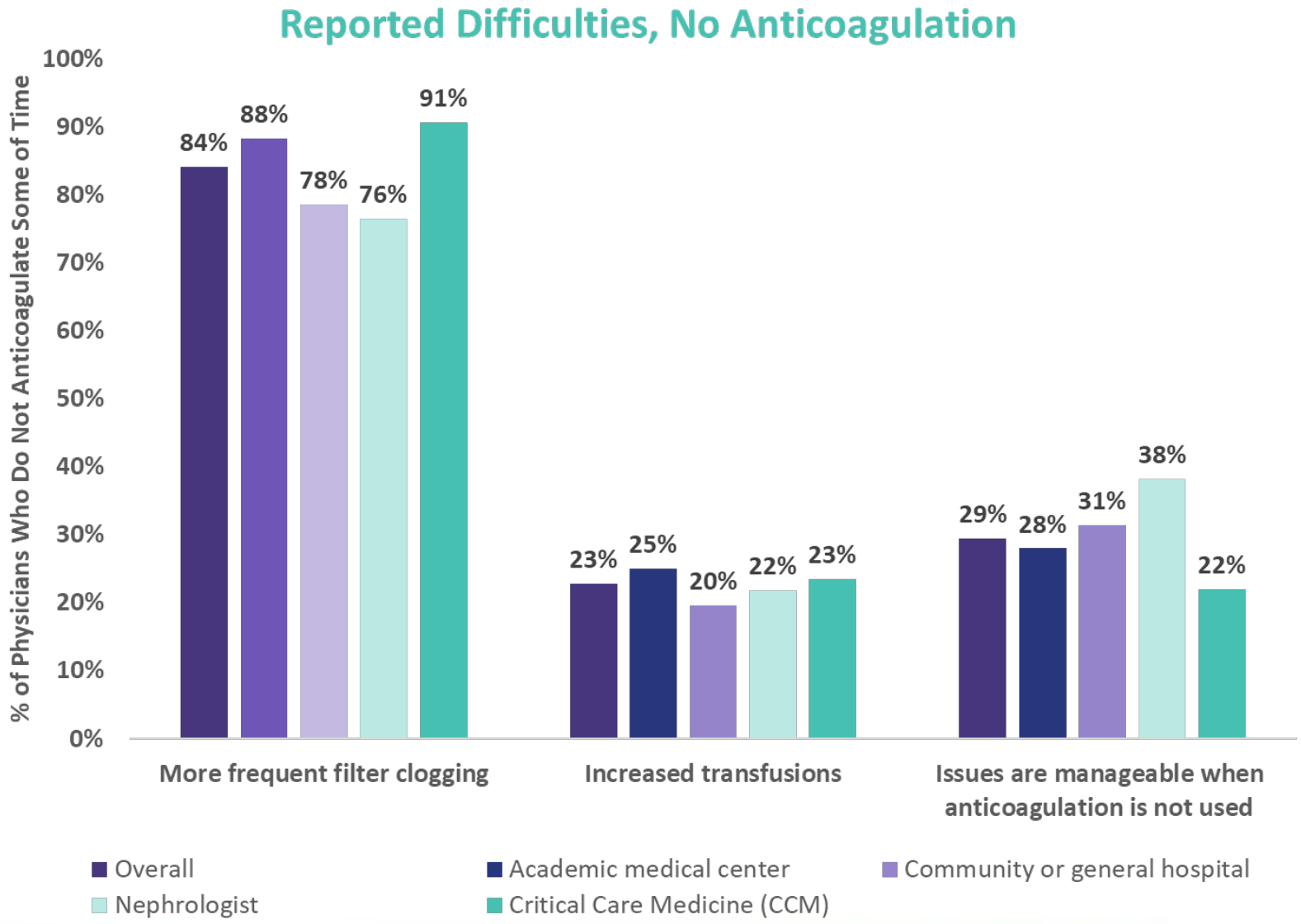
Citrate – 28%
(regional anticoagulant – anticoagulant for circuit only; used in U.S. under an Emergency Use Authorization)

No anticoagulant
29% is unfortunately the default when physicians are concerned with safety of heparin or citrate

Source: Boldt, et al. Anticoagulation practices for continuous renal replacement therapy: a survey of physicians from the United States, Renal Failure, 2023; https://doi.org/10.1080/0886022X.2023.2290932

TALPHERA

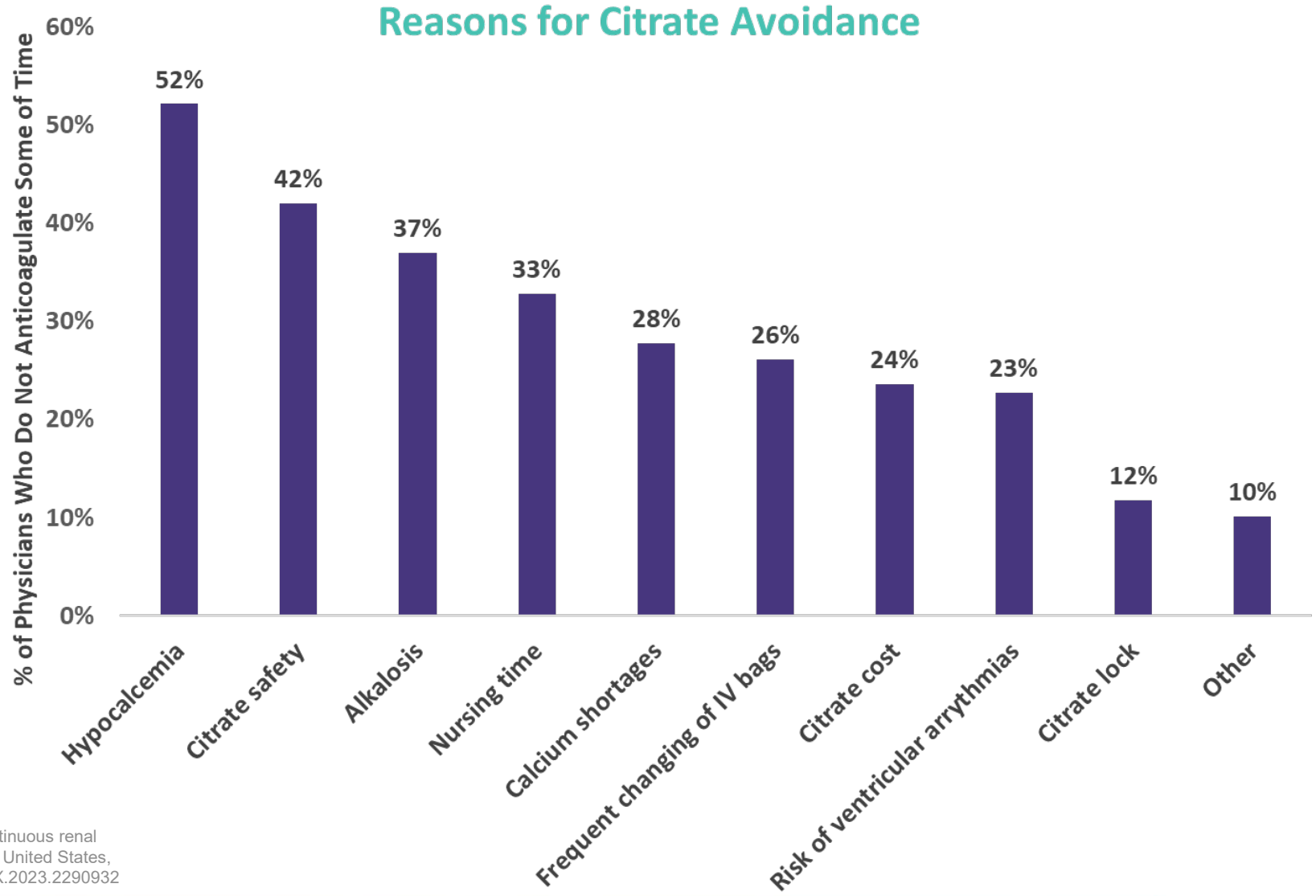
When not using an anticoagulant for CRRT, frequent filter clogging was the most common issue, with 20-25% stating increased transfusions were needed



Source: Boldt, et al. Anticoagulation practices for continuous renal replacement therapy: a survey of physicians from the United States, Renal Failure, 2023;https://doi.org/10.1080/0886022X.2023.2290932

TALPHERA

Market research indicated a number of reasons why physicians decide not to use citrate as an anticoagulant during CRRT despite it being given an EUA

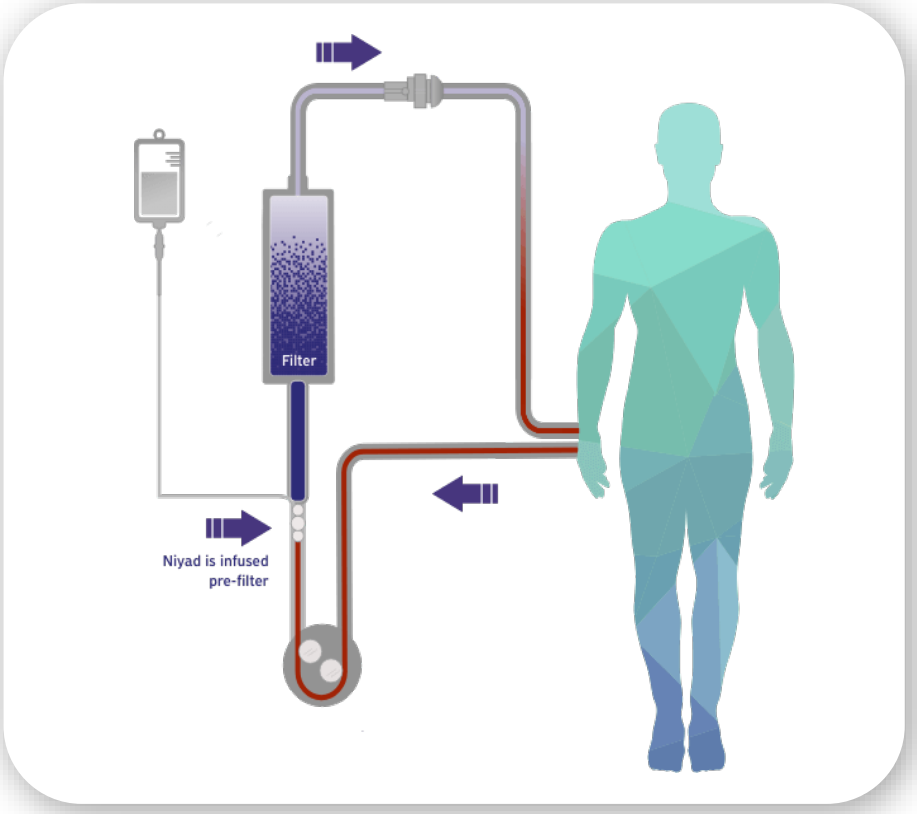


Source: Boldt, et al. Anticoagulation practices for continuous renal replacement therapy: a survey of physicians from the United States, Renal Failure, 2023;https://doi.org/10.1080/0886022X.2023.2290932

TALPHERA

Potential benefits of using Niyad in the dialysis circuit

- Standardized international guidelines recommend using an anticoagulant during renal replacement therapy (RRT)
- Niyad is designed to provide a short half-life, titratable, regional anticoagulation without the shortcomings of heparin or citrate
- Potential advantages of Niyad:
  - Niyad designed to be used in patients at risk of bleeding, whereas heparin is limited
  - Niyad designed to be used easily in patients with liver failure – whereas citrate is limited
- Compared to no anticoagulation: potential for fewer filter changes, fewer transfusions, more importantly – lower cost of doctor and nursing time



	Heparin	Nafamostat
Incidence of Bleeding[1]	66.7 %	4.3 %

1) Ohtake Y. Nafamostat as Anticoagulant in Continuous HD. Contrib Nephrol. 1991;93;215-217.

TALPHERA

Decades of use outside the U.S. and numerous studies support the benefits of nafamostat as an anticoagulant for the extracorporeal circuit

An independent, meta-analysis published in 2022 on the use of nafamostat as an anticoagulant in the extracorporeal circuit demonstrates the efficacy and safety compared to conventional therapy

11 Studies

2,723 Patients

Mortality

25% lower with nafamostat vs. conventional therapy (31% lower vs. no-anticoagulant)

Bleeding Risk

45% higher risk of bleeding complications on conventional therapy vs. nafamostat

Filter life

10.5 hours longer filter life compared to no-anticoagulant

Source: Yao Lin, et al; RENAL FAILURE, 2022, VOL. 44, NO. 1, 1263–1279, https://doi.org/10.1080/0886022X.2022.2105233

TALPHERA

FDA feedback on Niyad

Although an EUA for Niyad was not considered an FDA priority due to lack of FDA resources, correspondence with FDA provided us with encouraging feedback

FDA opined on 8/24/21:

"We believe that your device has the potential to address an unmet need in patients who cannot tolerate heparin or….who are treated in facilities that are ill-equipped for use of a citrate anticoagulant."

"Additionally, we recognize that there may be an unmet need for patients…who also cannot tolerate citrate due to another condition such as liver disease."

"We believe that you have provided significant evidence demonstrating that the potential benefits of the Niyad device could be greater than the reasonably foreseen risks."

Dr. Shakil Aslam, our new Chief Medical Officer as of October 2024

Shakil Aslam, MD is a nephrologist with over 20 years of experience in academia, patient care, basic and clinical research and drug and device safety and development. He joined Talphera from BioCryst Pharmaceuticals where he was the Vice President, Clinical Development, Nephrology and Rare Diseases. Dr. Aslam previously held roles at Angion Biomedica, Fresenius Medical Care and Amgen and was an assistant professor at Georgetown University hospital for twelve years with a focus on acute and chronic kidney disease, hypertension, and other kidney diseases. He has authored over two dozen articles in peer-reviewed journals and several book chapters.

TALPHERA

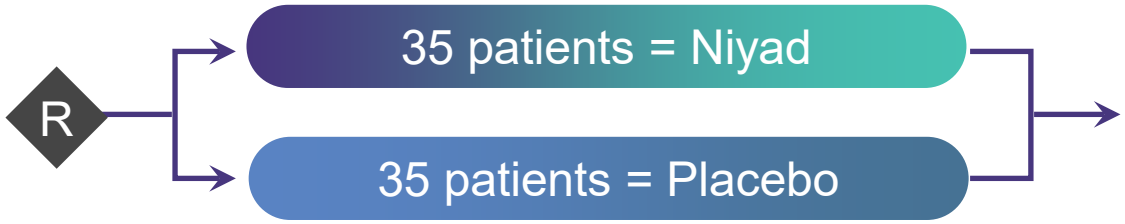
Single registrational study on Niyad

Prospective, randomized, placebo-controlled study at up to 14 clinical sites

Randomization

70* adult patients undergoing RRT who cannot tolerate heparin or are at risk for bleeding

Dosing period (7 days)



Primary Endpoints:

- Mean post-filter activated clotting time (ACT) over first 24 hours versus placebo

Key Secondary Endpoints:

- Mean post-filter ACT over 72 hours
- Filter lifespan
- Number of filter changes over 72 hours
- Number of transfusions over 72 hours
- Dialysis efficacy (based on urea concentration) over first 24 hours

Safety

Bleeding, electrolyte disorders, 28-day all-cause mortality

** FDA approved a reduction from 166 patients as announced in March 2025; primary endpoint still powered at 90%*

TALPHERA

Study enrollment rate has accelerated with 35 patients enrolled through March 2

Enrollment expected to be completed in 2026

Enrollment rate acceleration driven by target profile sites brought on at the end of 2025, with the final target profile sites activated in Q1 2026

35

Patients enrolled through March 2, 2026 (last public disclosure)

12

Total activated sites screening patients

8

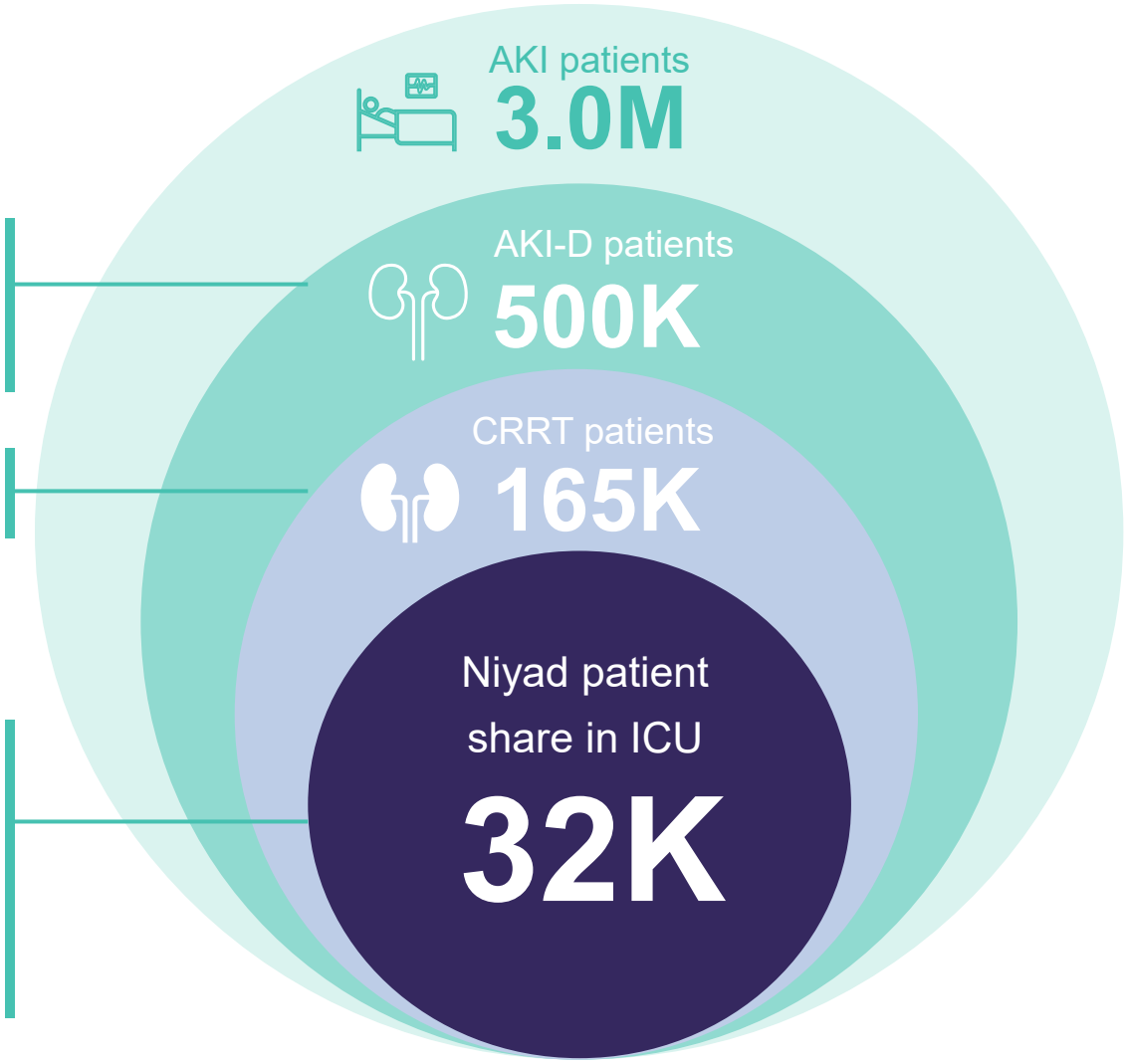
Target profile sites screening patients

New profile sites are expected to be highest enrolling, currently covering over 90% of enrollment to date

TALPHERA

Niyad™ market opportunity in CRRT

If approved, Niyad would be the only FDA approved regional anticoagulant for the extracorporeal circuit



Some patients receive intermittent hemodialysis (IHD) and others continuous (CRRT)

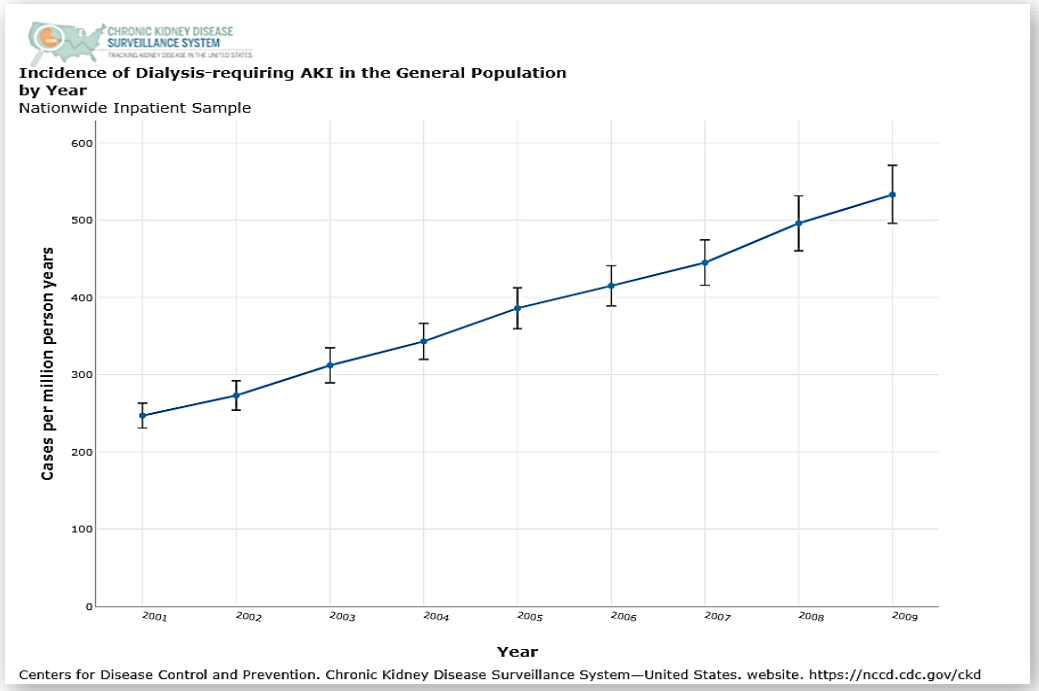
5-7 days average CRRT; then possible transition to IHD

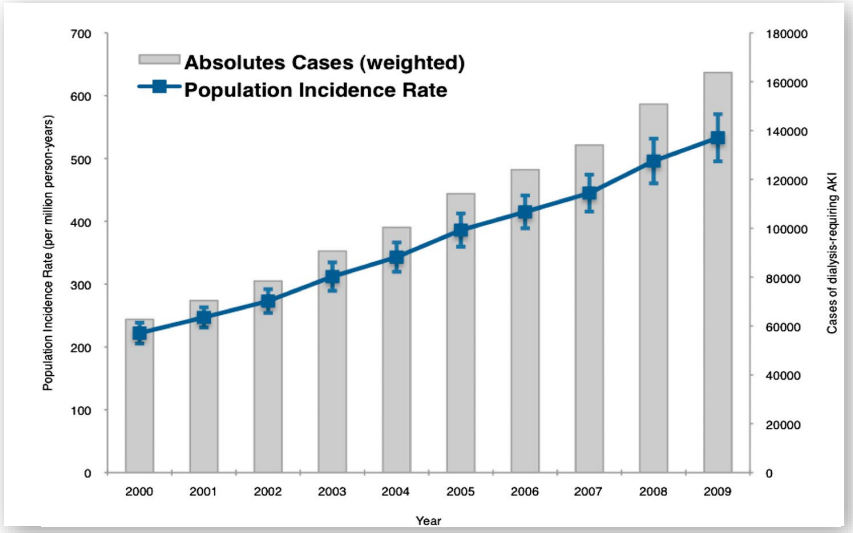
Estimated 19.5% share taken from (a) no anticoagulant used because of safety with current products; (b) some from heparin and (c) some from citrate.

Total patient numbers excludes other in-hospital anticoagulation of extracorporeal circuits (ECMO, CRRT outside of ICU)

TALPHERA

Acute kidney injury rates are rapidly increasing

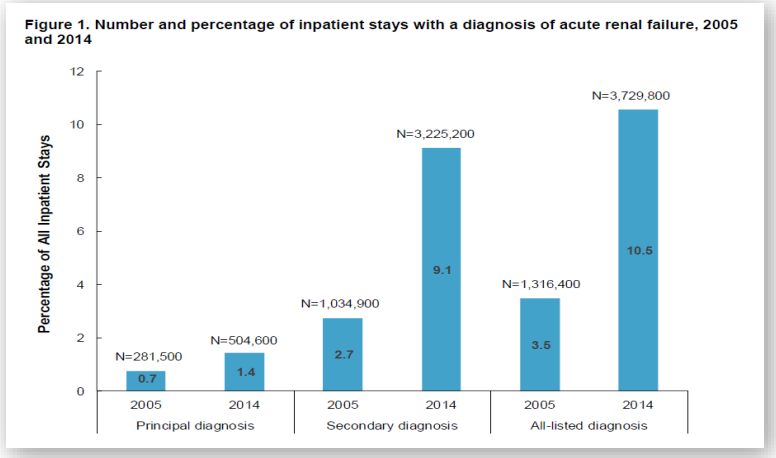




Hsu RK, McCulloch CE, Dudley RA, Lo LJ, Hsu CY. Temporal changes in incidence of dialysis-requiring AKI. J Am Soc Nephrol. 2013;24(1):37-42.

Acute kidney injury (AKI) is defined by a rapid increase in serum creatinine, decrease in urine output, or both. AKI occurs in approximately 10-15% of patients admitted to hospital, while its incidence in intensive care has been reported in more than 50% of patients.[1]

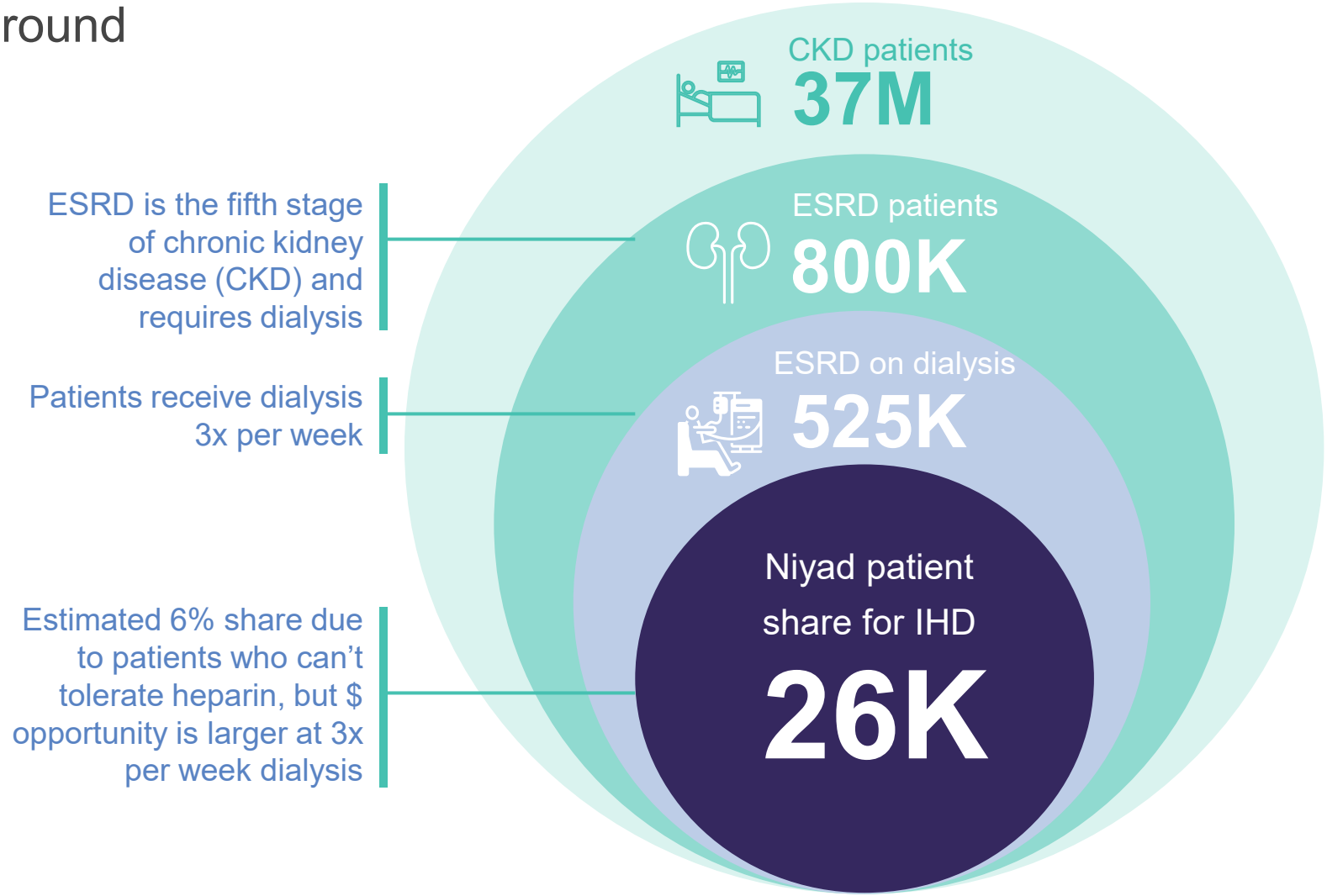
Note: Diagnoses were identified using the Clinical Classifications Software (CCS). Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), National (Nationwide) Inpatient Sample (NIS), 2005â€“2014



1. Acute kidney injury. Lancet. 2019; 394(10212):1949-1964 (ISSN: 1474-547X), Ronco C; Bellomo R; Kellum JA

Niyad™ market opportunity in IHD

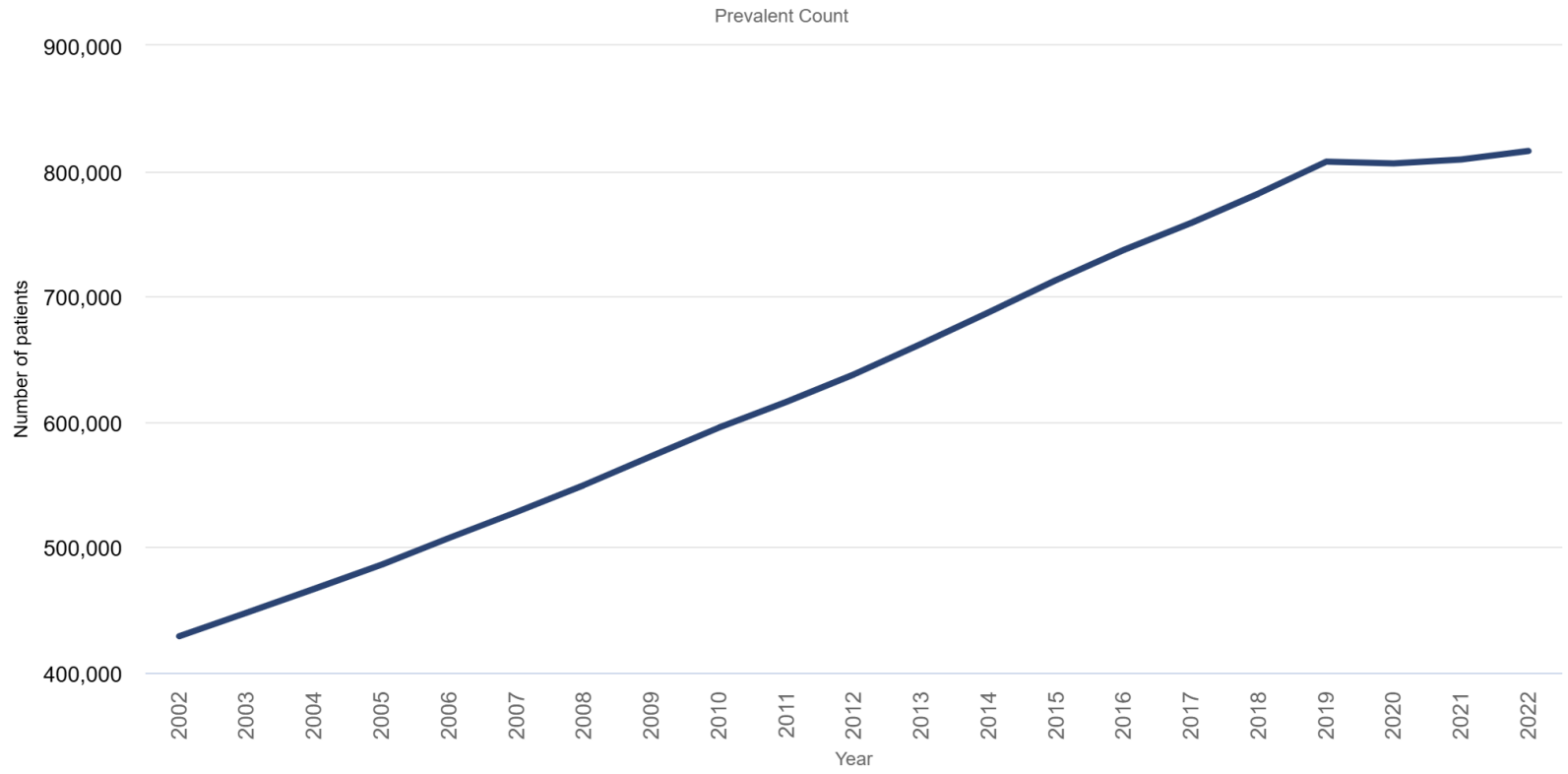
Intermittent hemodialysis is shorter in duration than CRRT, however, frequency of the procedure is 3x per week, year-round



TALPHERA

End stage renal disease (ESRD) continues to increase

Figure 1.7 Prevalence of ESRD, 2002-2022



Data Source: 2024 United States Renal Data System Annual Data Report

End stage renal disease (ESRD) is the fifth stage of chronic kidney disease (CKD) and requires dialysis or transplant

TALPHERA

LTX-608: the other nafamostat opportunity with broad potential

Nafamostat is a "pipeline in a product" that has potential beyond Niyad

Disseminated intravascular coagulation (DIC)

Approved indication in Japan and South Korea; intellectual property protection will focus on method of use patents based on the complexity of DIC treatment

Acute pancreatitis

Approved indication in Japan and South Korea

Acute respiratory distress syndrome (ARDS)

A life-threatening lung injury that allows fluid to leak into lungs; Nafamostat potential modes of action of anticoagulation, anti-inflammation and sustaining endothelial barrier function/preventing vascular leak could support exploring development

Anti-viral

Various ex-US studies have demonstrated positive results; publications support development as a potential COVID treatment by inhibiting TMPRSS2; A potent broad-spectrum serine protease inhibitor that blocks host protease activation of the viral spike protein [1]

1. B. F. Niemeyer, C. M.Miller, C. Ledesma-Feliciano, J. H. Morrison, R.Jimenez-Valdes,C.Clifton,E.M.Poeschla,K.H.Benam, Nano Select □□□□

TALPHERA

Nafamostat intellectual property status and data exclusivity

Potential for six years data exclusivity upon Niyad PMA approval before issuance of pending patents

Niyad™ patent pending

Claims drawn to priming of the extracorporeal circuit and blood flow when using nafamostat.

PCT patent applications filed in January 2025; Various national patents expected to be filed before mid-2026

TALPHERA

Financial information/metrics

$20.4M
December 31, 2025 cash and investments

$17-18M
FY 2026 estimated cash operating expense (excludes stock-based compensation)

$3.5M
Q4 2025 combined R&D and SG&A(1)

(1) Operating expenses: Combined R&D and SG&A including $0.2M non-cash stock-based compensation

TALPHERA

TALPHERA

Innovative products for medically supervised settings

Nasdaq: TLPH