



Innovative products for medically supervised settings

Nasdaq: ACRX

October 2023

Forward-looking statements and non-GAAP financial measures

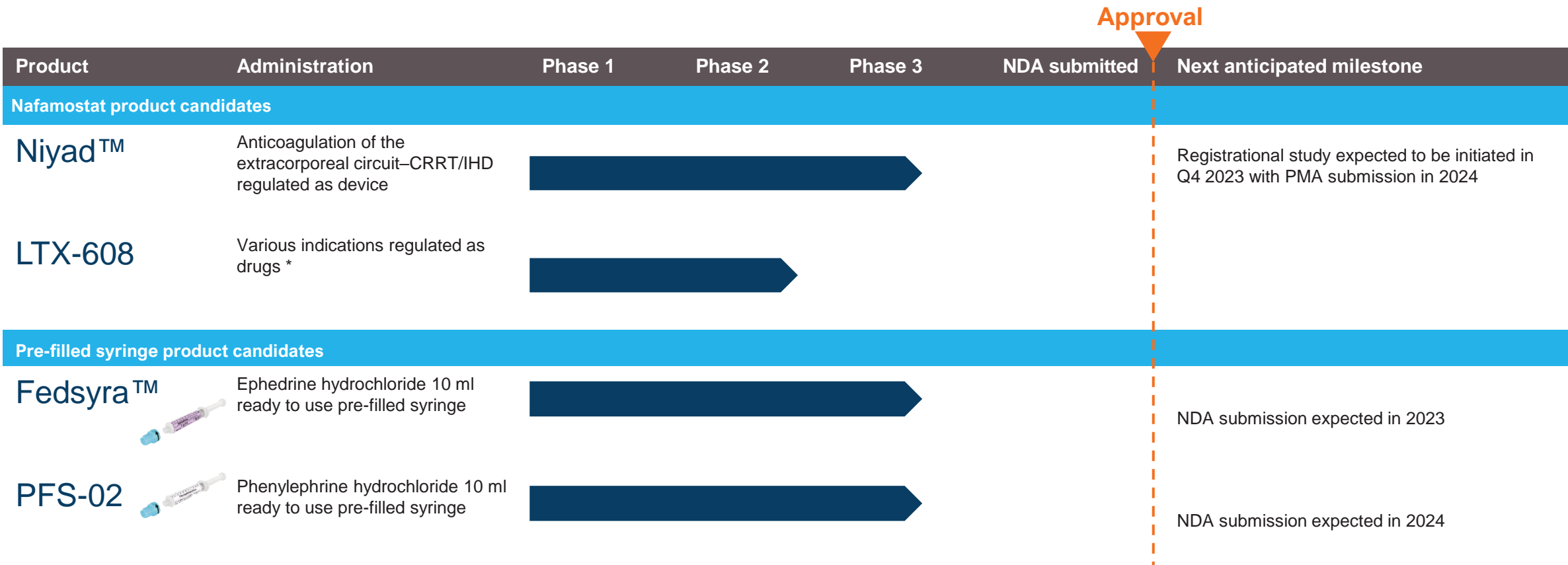
Forward-Looking Statements

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.acelrx.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 AcelRx’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.

Portfolio Overview



DSUVIA®
(sufentanil)
sublingual tablet 30 mcg



Divested to Alora Pharmaceuticals, and due **15%** royalties on commercial sales; **75%** royalties on sales to the Department of Defense, and up to **\$116.5M** in milestone payments; Transaction closed in April 2023

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

AcelRx Investment Highlights

1

Late-stage pipeline assets with near-term commercial potential in medically supervised settings

2

Lead asset Niyad has FDA Breakthrough Designation with potential peak sales of \$200M

3

Single registrational study for Niyad planned to begin enrolling in Q4 2023; 166 total patient study, expected 6-8 months timing followed by PMA submission in 2024; we believe high probability of success

4

Fedsyra™, ephedrine pre-filled syringe NDA submission expected in H2 2023

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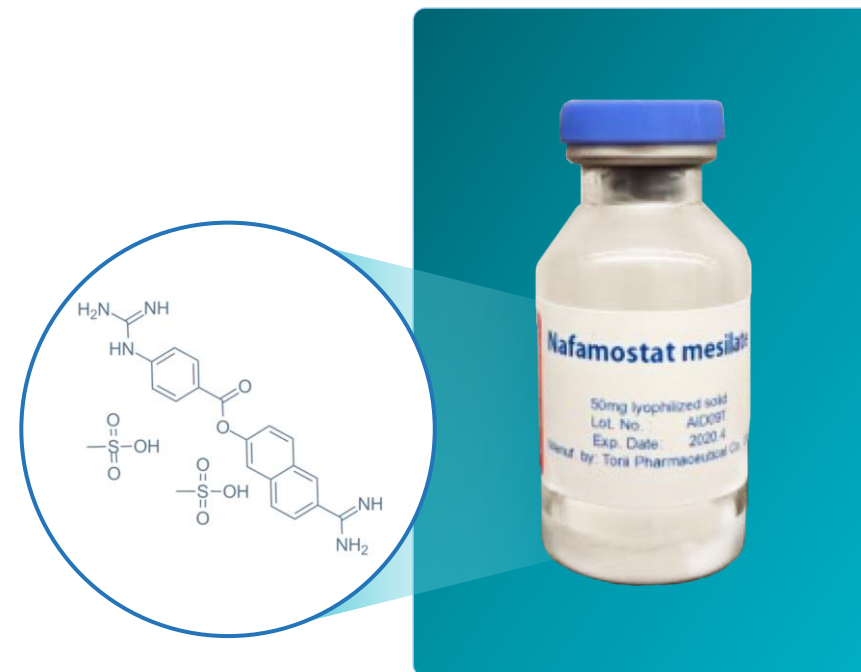
Royalty stream from April 2023 divestment of DSUVIA to Alora Pharmaceuticals - 15% on commercial sales, 75% on DoD sales and up to \$116.5M in milestones



Niyad™ and LTX-608

What is nafamostat?

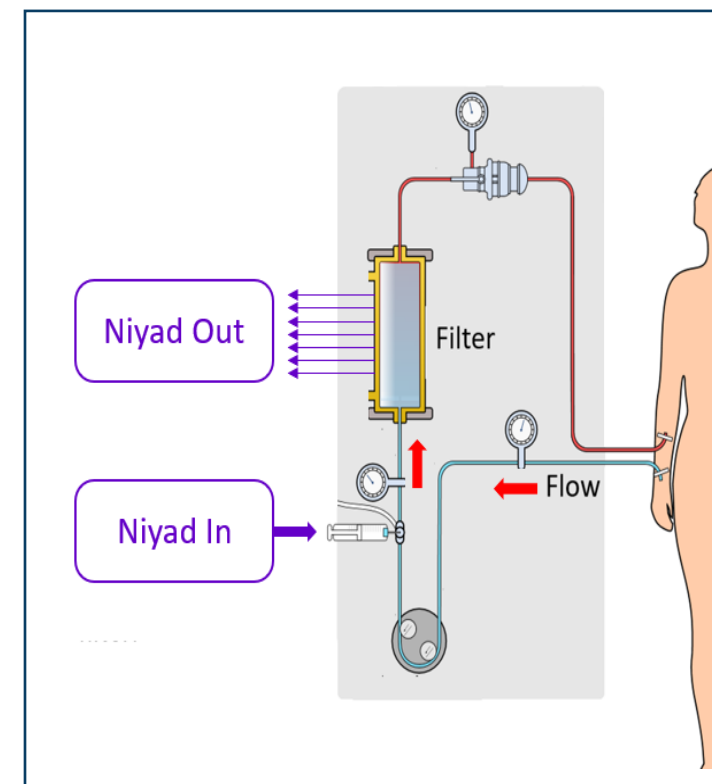
- An investigational broad-spectrum serine protease inhibitor with anticoagulant, anti-inflammatory, mucus clearing and potential anti-viral activities
- Half-life of 8 minutes
- Multiple potential indications given its proposed mechanism of action
- Approved and used in Japan and South Korea for over 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

AcelRx 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 (as it works in the circuit and not the body)
 - 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
- ✓ Approval for a **single registrational study** planned to start in Q4 2023 with endpoints agreed with the FDA
- ✓ ICD-10 CMS procedural code already received for **reimbursement**
- ✓ Niyad peak sales estimated at more than **\$200 million**



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 resources¹. Circuit clotting is the most frequent cause of therapy interruption circuit dialysis²



More frequent filter changes required to ensure efficacy



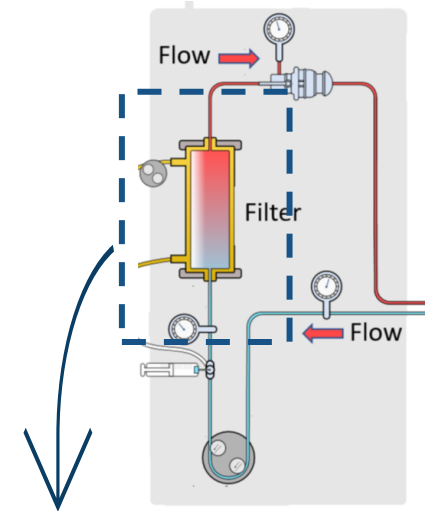
Increased blood loss; increased platelet transfusions



Delayed/prolonged treatment time



Burden on healthcare professional

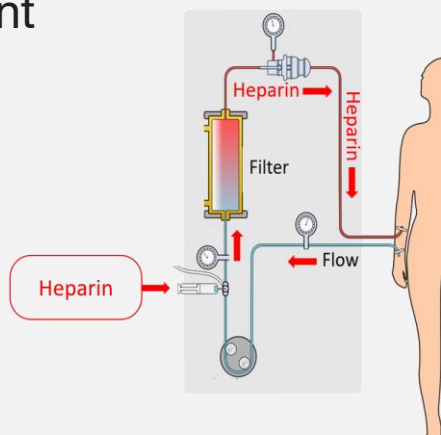


1. Uchino S, Fealy N, Baldwin I, Morimatsu H, Bellomo R. Continuous is not continuous: the incidence and impact of circuit “down-time” on uraemic control during continuous veno-venous haemofiltration. *Intensive Care Med.* 2003;29:575–578. Zhang Z, Ni H, Lu B. Variables associated with circuit life span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

Current standards for anticoagulation have many disadvantages

Heparin

- Systemic anticoagulant
- Prolonged half-life up to 6 hours makes it difficult to titrate
- Clinicians fear over anticoagulating the patient
- Significant safety concern for patients at risk of bleeding
- Thrombocytopenia



Citrate

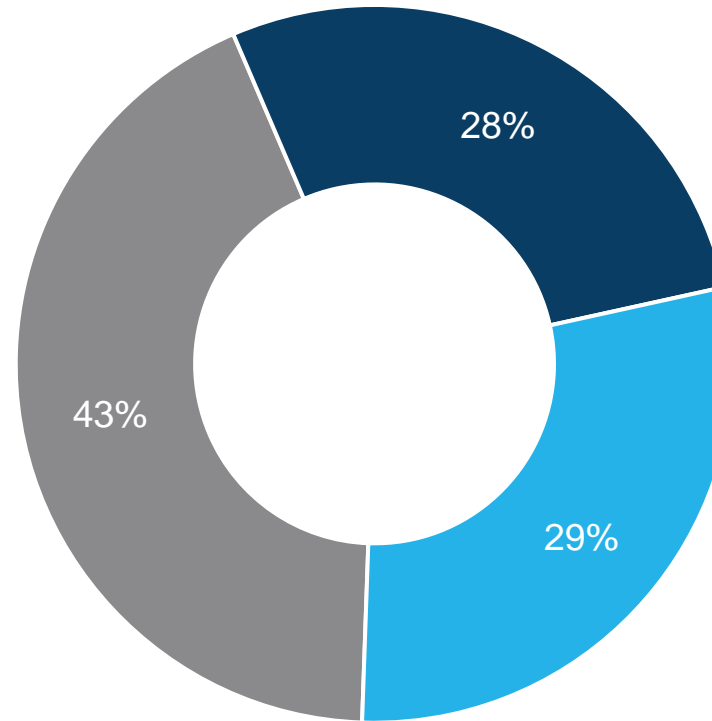
- Citrate chelates calcium, which inhibits the generation of thrombin
- Using citrate requires infusing calcium on the return side of filter (back to patient)
- Extensive, complicated protocol
- Frequent blood draws to measure calcium are time-consuming and expensive
- Rapid changes in calcium levels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



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%

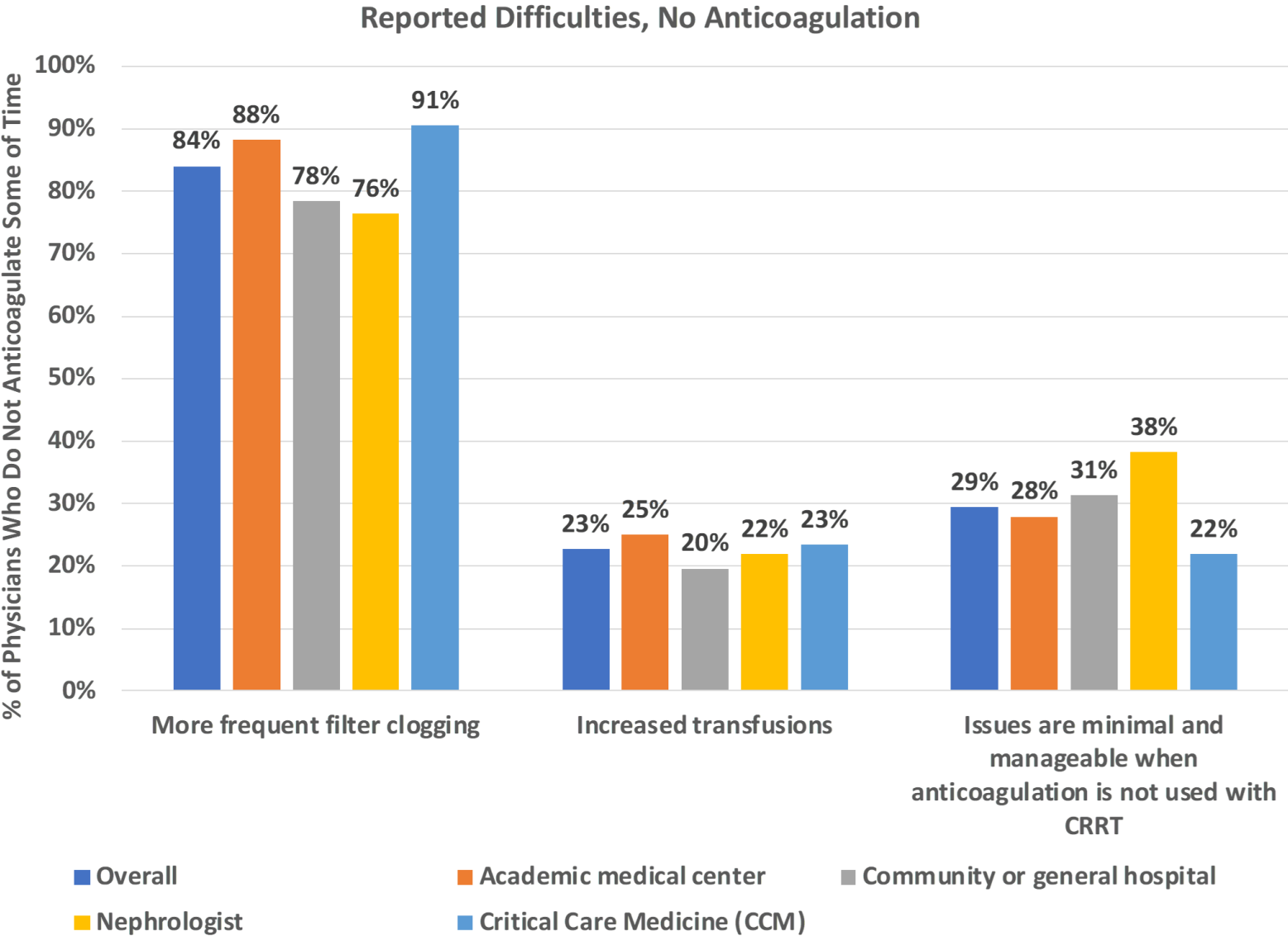
(regional anticoagulant – anticoagulant for circuit only; used in U.S. under an Emergency Use Authorization)

No anticoagulant

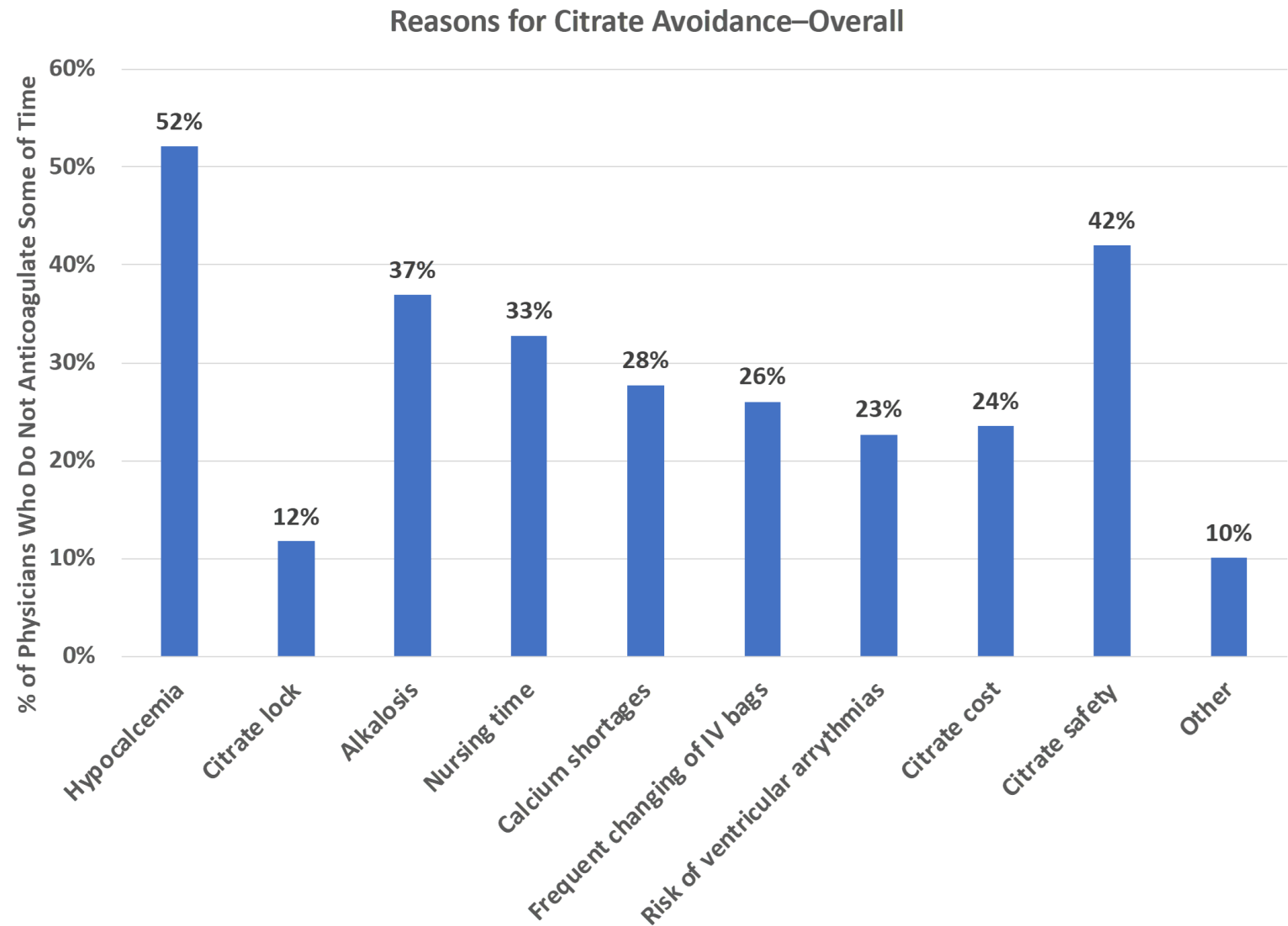
29% is unfortunately the default when physicians are concerned with safety of heparin or citrate

■ Heparin ■ Citrate ■ No anticoagulant

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

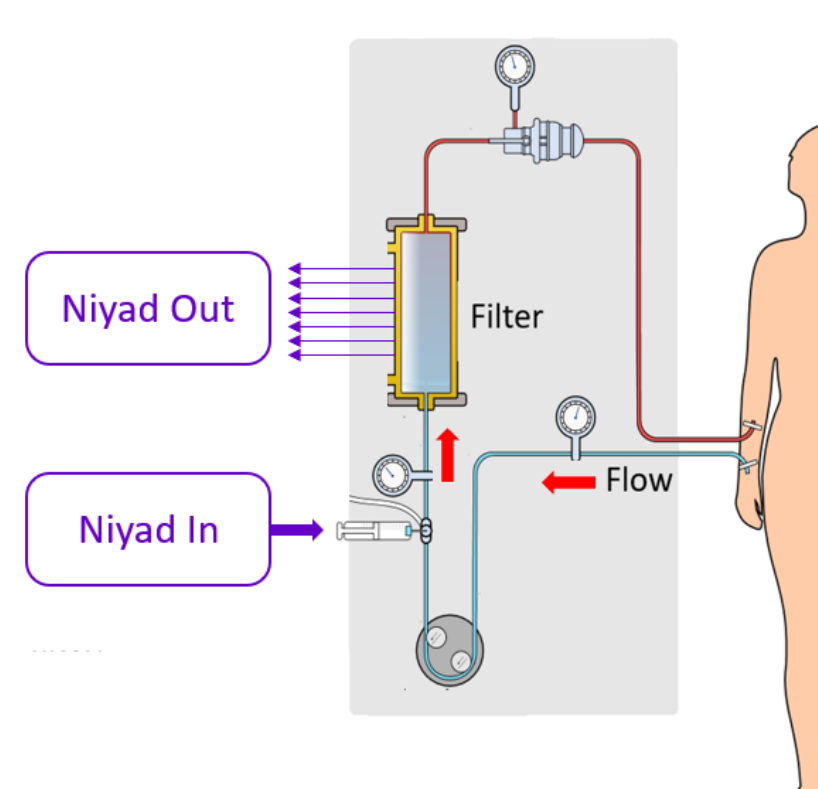


Market research indicated a number of reasons why physicians decide not to use citrate as an anticoagulant during CRRT despite it being given an EUA



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 %

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

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

2,723
patients

FDA feedback on Emergency Use Authorization (EUA) for Niyad

Although 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.”

Single registrational study on Niyad

FDA has approved the IDE with a single registrational study being initiated in Q4 2023

Prospective, randomized, placebo-controlled study at up to 10 clinical sites

Randomization

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

R

Dosing period (7 days)

83 patients = Niyad

83 patients = Placebo

Safety:

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

Primary Endpoints:

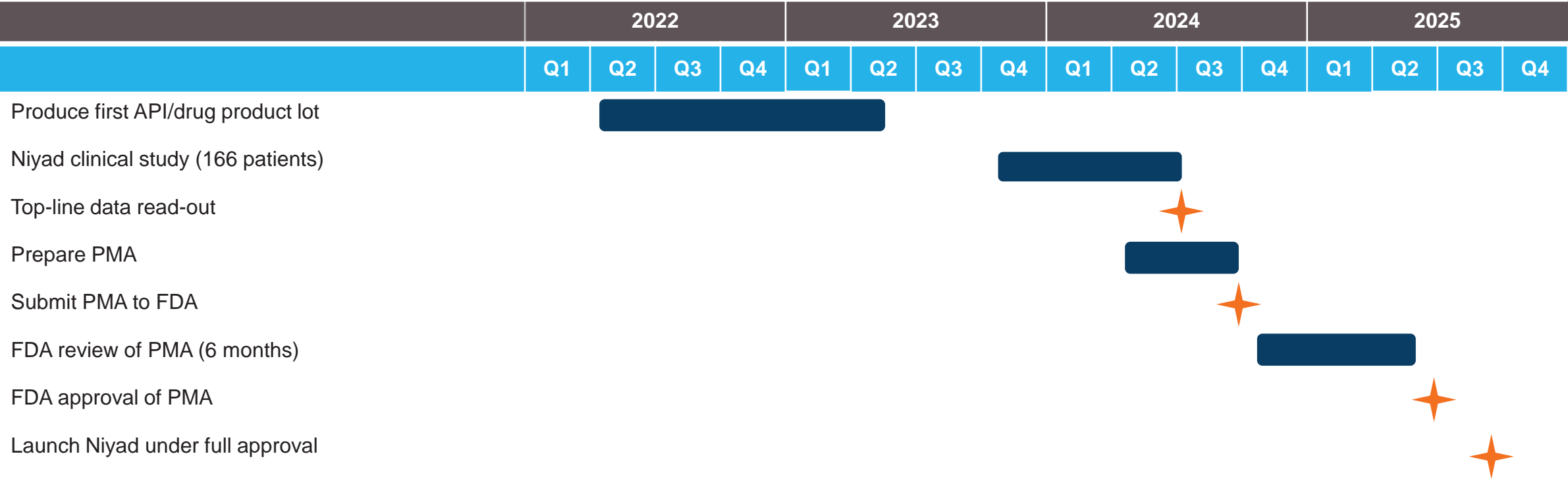
- mean post-filter activated clotting time (ACT) over first 24 hours versus placebo

Key Secondary Endpoints:

- 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

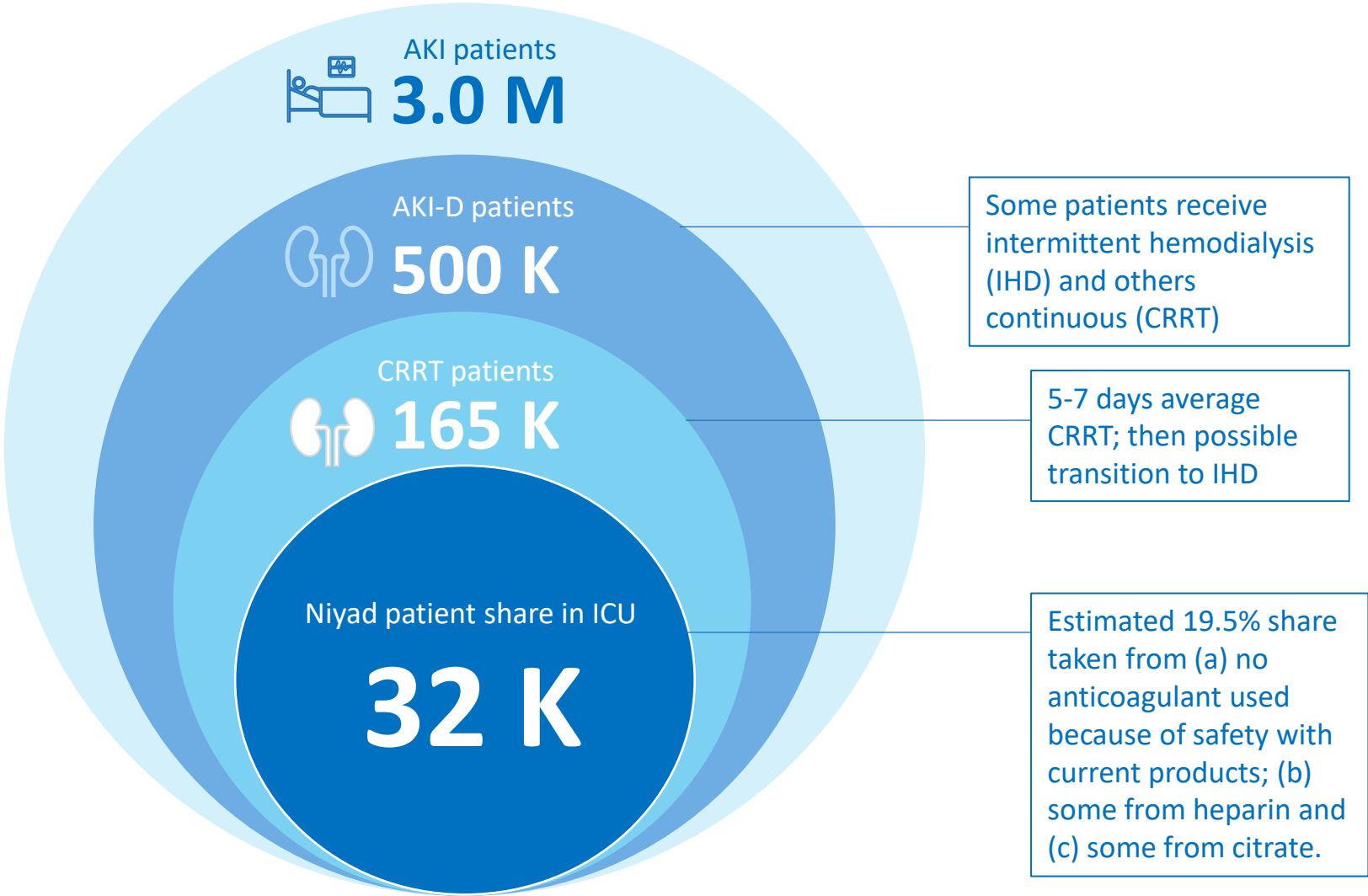
Anticipated timeline to PMA approval for Niyad™

FDA review of IDE is complete with approval for a single study of 166 patients with primary and secondary endpoints established



Niyad™ market opportunity in CRRT

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

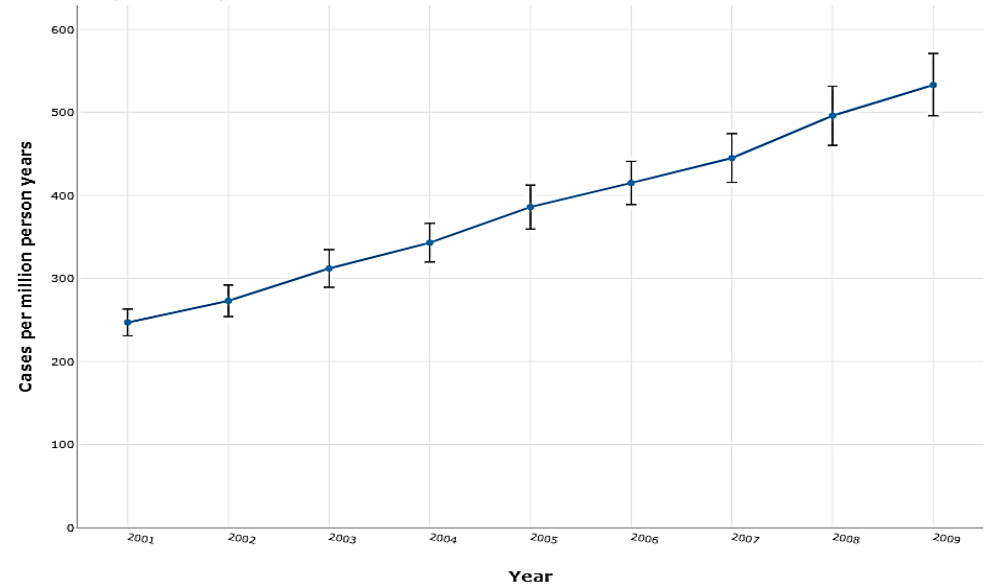


Excludes other in-hospital anticoagulation of extracorporeal circuits (ECMO, CRRT outside of ICU)

Acute kidney injury rates are rapidly increasing

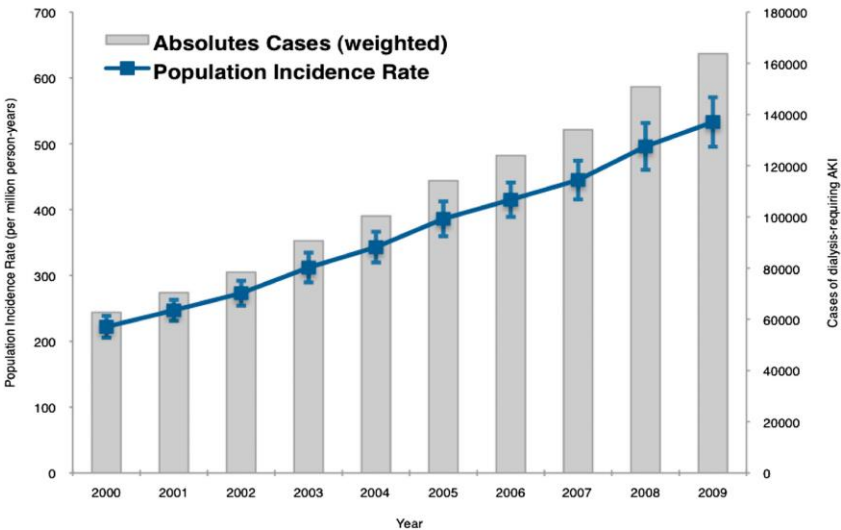


Incidence of Dialysis-requiring AKI in the General Population by Year
Nationwide Inpatient Sample



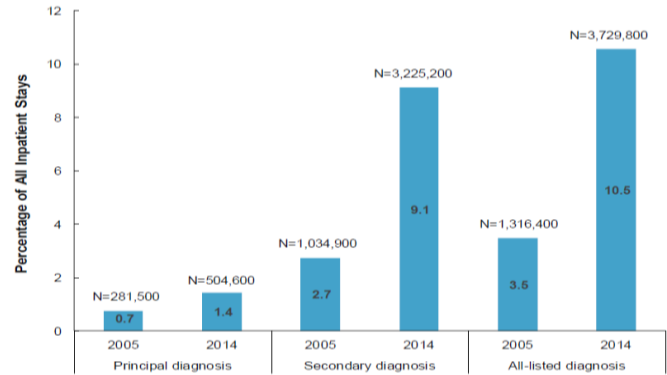
Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. <https://nccd.cdc.gov/ckd>

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



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.

Figure 1. Number and percentage of inpatient stays with a diagnosis of acute renal failure, 2005 and 2014

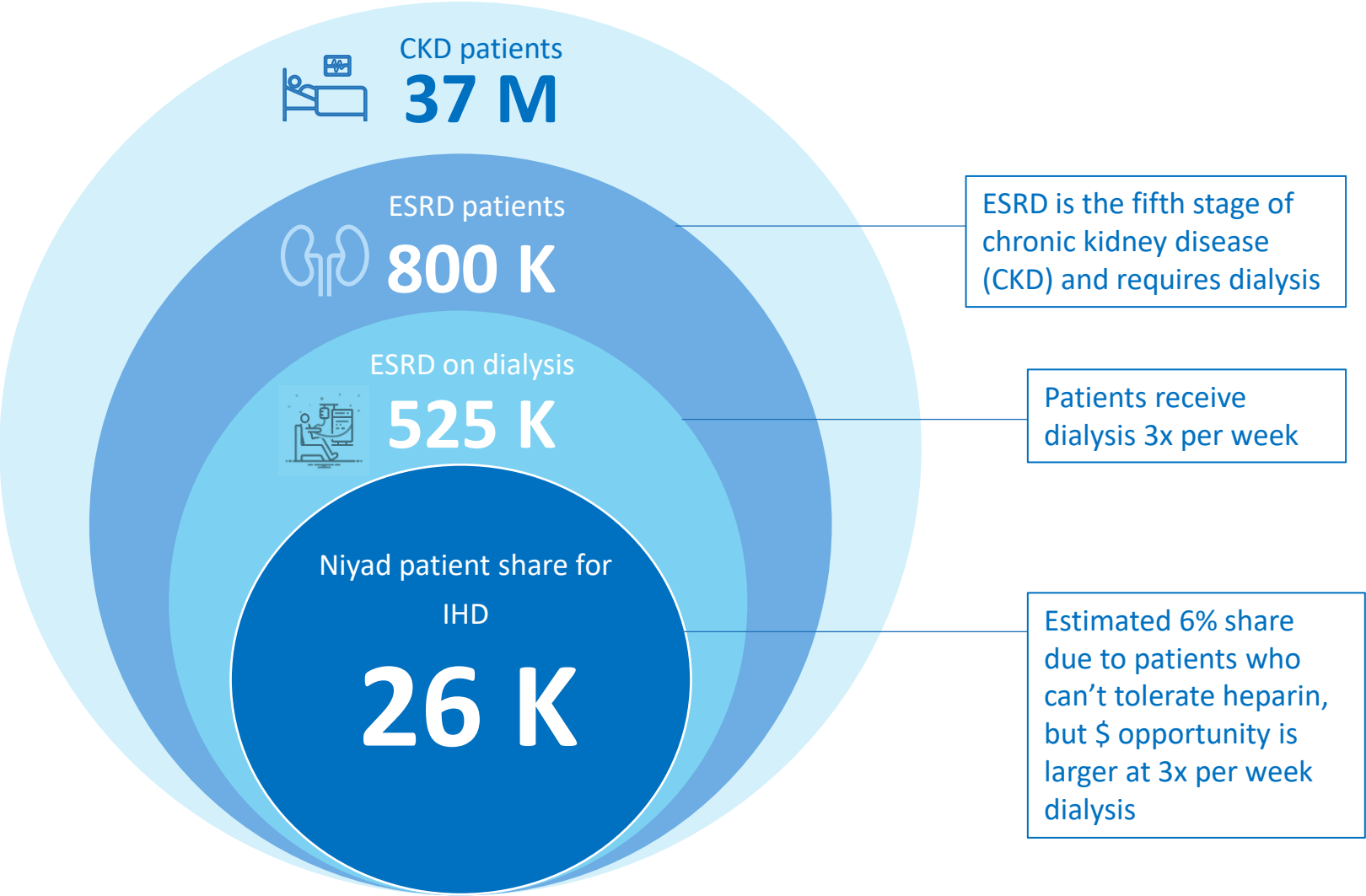


Note: Diagnoses were identified using the Clinical Classifications Software (CCS).
Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), National (Nationwide) Inpatient Sample (NIS), 2005–2014

1. Acute kidney injury. [Lancet. 2019; 394\(10212\):1949-1964](https://doi.org/10.1016/S0140-6736(19)30443-6) (ISSN: 1474-547X), Ronco C; Bellomo R; Kellum JA

Niyad™ market opportunity in IHD

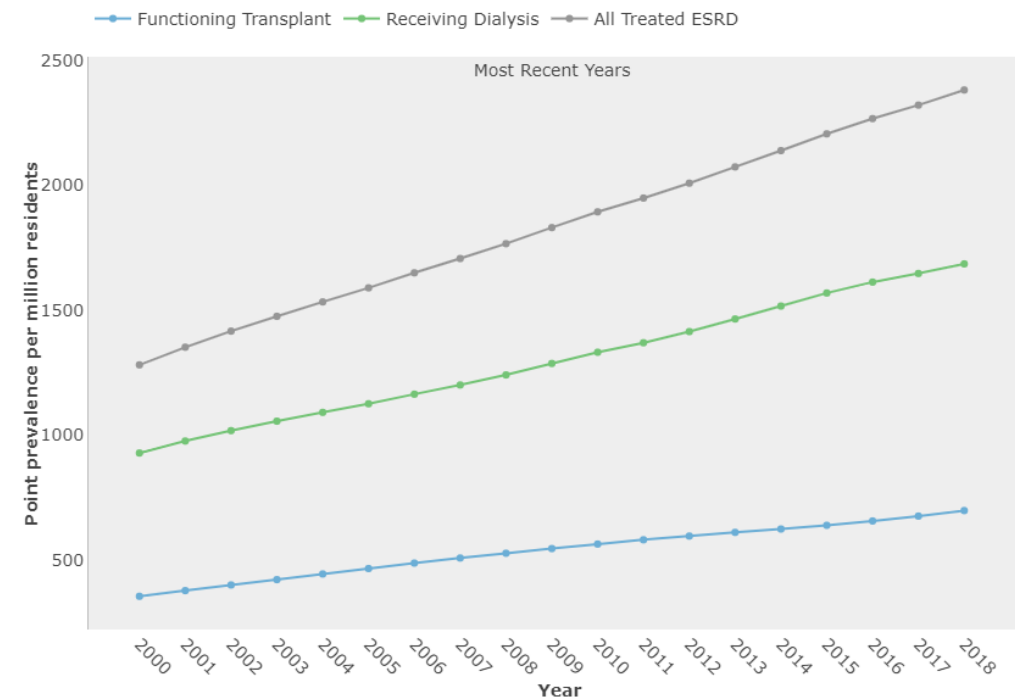
Intermittent hemodialysis is shorter in duration than CRRT, however, frequency of the procedure is 3x per week, year-round



End stage renal disease (ESRD) and outpatient dialysis continues to increase

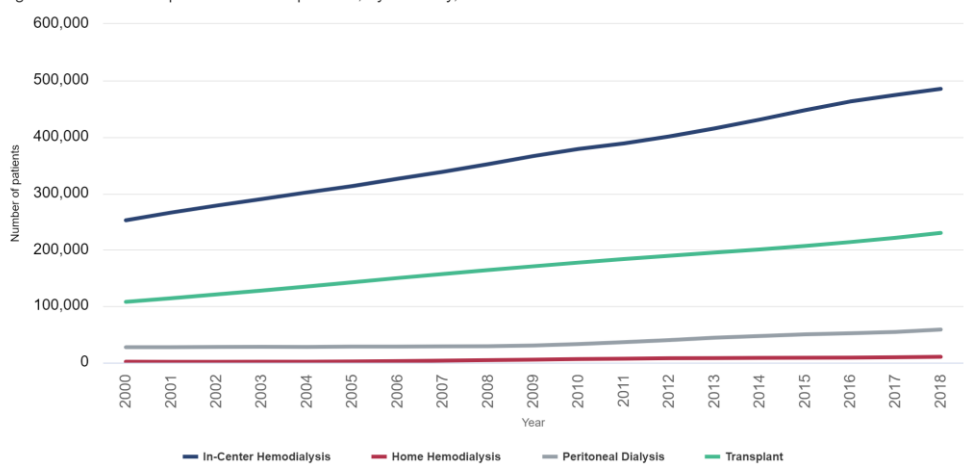


Prevalence of Treated End-Stage Renal Disease (ESRD) per Million U.S. Residents
by Most Recent Years and Year and Treatment
United States Renal Data System



Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. <https://nccd.cdc.gov/ckd>

Figure 1.6 Number of prevalent ESRD patients, by modality, 2000-2018



Data Source: 2020 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; The prevalence of ESRD has more than tripled since 1990 ¹



1. Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. <http://www.cdc.gov/ckd>

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

COVID treatment

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
Lowell has a published patent regarding nafamostat antiviral for COVID and others

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

Acute pancreatitis

Approved indication in Japan and South Korea

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.

LTX-608 (nafamostat) multiple patents pending

Claims drawn to use of nafamostat in disseminated intravascular coagulation (DIC), as an antiviral agent (e.g., COVID treatment), in acute respiratory distress (ARDS) and other conditions.

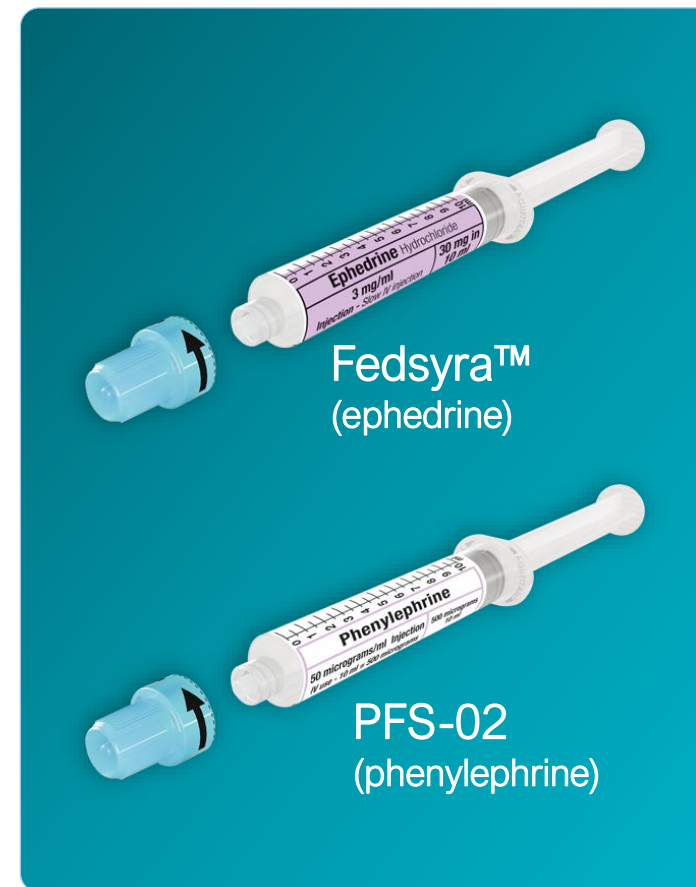


Pre-filled syringe portfolio

Fedsyra™ - Ephedrine hydrochloride 10 ml pre-filled syringe
Phenylephrine hydrochloride 10 ml pre-filled syringe

Two complementary pipeline products added in July 2021 through a licensing agreement with France-based pharmaceutical company Laboratoire Aguettant

- Pre-filled, ready-to-use syringes of commonly used products for acute care
- Pre-filled, ready-to-use ephedrine and phenylephrine syringes combined market opportunity is estimated at over \$100 million
- Minimal expected cost to get the products through NDA submissions and potential approval
- NDA submission for ephedrine expected in 2023 and phenylephrine expected in 2024
- Approved and marketed products in Europe and other regions outside the U.S.



Ephedrine and phenylephrine: Commonly used medicines in the perioperative settings for hypotension

Ephedrine is a first-line treatment for hypotension under general anesthesia¹

Ephedrine is an alpha- and beta- adrenergic agonist and a norepinephrine-releasing agent that is indicated for the treatment of clinically important hypotension occurring in the setting of anesthesia



Generic
concentrate vial



Ready-to-use
vial/ampoule



Ready-to-use
Syringe *

Phenylephrine is a first line treatment for hypotension for obstetrics and spinal anesthesia²

Phenylephrine is an alpha-1 adrenergic receptor agonist for the treatment of clinically important hypotension resulting primarily from vasodilation in the setting of anesthesia



*Evolving to
pre-filled syringes*

Aguettant pre-filled syringes are focused on delivering commonly used medicines safely and efficiently

- Perioperative medication errors continue, and pre-filled syringes are preferred for improving safety while containing costs
- Ready to use vials of ephedrine and phenylephrine were recently approved: Emerphed (in 2020), Eton, Nevakar; Pre-filled ephedrine syringes were recently approved (in 2022 and 2023): Akovaz, Emerphed

Per Patient Saf Advis 2018 Dec;15(4).

Perioperative Medication Errors: Uncovering Risk from Behind the Drapes

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Abstract

Medication use in the perioperative setting presents unique challenges. For example, perioperative medication prescribers, such as electronic physician order entry with administration, and multiple nursing checks at the time events associated with the perioperative settings (e.g., identified by analysts in event reports to the Pennsylvania Patient Safety Authority). More than half (54.6%, n = 621) of reported events were attributed to a breakdown in the communication. Other common contributing factors involve improper handling of medications leading to mix-ups. Organizations may use this data to inform proactive efforts to prevent similar errors from occurring.

Introduction

Although medication errors are preventable, they occur 600,000 to upwards of \$5.6 billion per hospital each year. High-stress surgical procedure management compared with general medical-surgical patient care is

PERIOPERATIVE MEDICINE

Evaluation of Perioperative Medication Errors and Adverse Drug Events

Karen C. Nangl, M.D., M.P.H., Amit Patel, M.D., M.P.H., Sofia Shukh, B.Sc., Diane L. Seger, R.Ph., David W. Bates, M.D., M.Sc.

ABSTRACT

Background: The purpose of this study is to assess the rates of perioperative medication errors (MEs) and adverse drug events (ADEs) as percentages of medication administrations, to evaluate their root causes, and to formulate targeted solutions to prevent them.

Methods: In this prospective observational study, anesthesia-trained study staff (anesthesiologists/nurse anesthetists) observed randomly selected operations in a 1,000-bed tertiary care academic medical center to identify MEs and ADEs over 8 months. Retrospective chart abstraction was performed to flag events that were missed by observation. All events subsequently underwent review by two independent reviewers. Primary outcomes were the incidence of MEs and ADEs.

Results: A total of 277 operations were observed with 3,603 medication administrations of which 223 (3.3%), 298 (3.4%), 5 (0.1%) involved a ME and/or ADE. Of these, 144 (78.0%) were preventable and 40 (20.7%) were nonpreventable. The events included 153 (79.5%) errors and 94 (50.8%) ADEs. Of the 153 errors, 133 (87%) were preventable and 20 (13%) were nonpreventable. Of the 94 ADEs, 50 (53.2%) were preventable and 44 (46.8%) were nonpreventable.

Conclusions: One in 20 perioperative medication administrations resulted in a ME or ADE. The most common MEs led to observed ADEs, and the most common ADEs reported by retrospective surveys. Based on MEs, *(American Journal of Perioperative Medicine 2019; 124:21-28)*

NEWS RELEASE

March 18, 2021

ISMP Launches Perioperative Medication Safety Self Assessment

New Tool Will Help Surgery Sites Evaluate, Document Compliance, Compare Scores/Performance, Fix Medication Errors Happen in all phases of perioperative care, often due to the complexity and fast-paced nature of the setting, as well as the multiple handoffs of care. The Institute for Safe Medication Practices (ISMP) has released a new assessment to help hospitals, ambulatory surgical centers, and other surgery settings evaluate their medication safety practices and identify specific challenges and opportunities for improvement.

CONTACT
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rbreslin@ismp.org • 614-376-0212

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Prefilled Syringes Are the Preferred Choice

Waste reduction, time-savings and increased safety are among the benefits of purchasing preloaded medications.

Sheldon Sones

Publish Date: April 8, 2021 | Tags: Supply Management (/outpatient-surgery/search#sort=date%20descending&f=osmtopicfacet=Supply Management)

QUICK DRAW Prefilled syringes allow you to bypass the time-consuming task of drawing up medications and complying with safe labeling practices. | Pamela Bevelhymmer

AcelRx
Pharmaceuticals, Inc.

| 27



DSUVIA was divested to Alora Pharmaceuticals in April 2023 with long-term value creation expected from royalties and milestones

DSUVIA[®]
(sufentanil)
sublingual tablet 30 mcg (II)

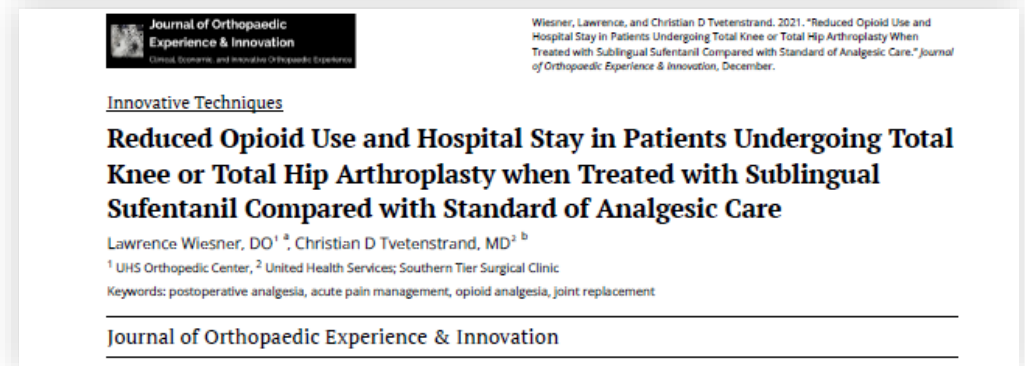
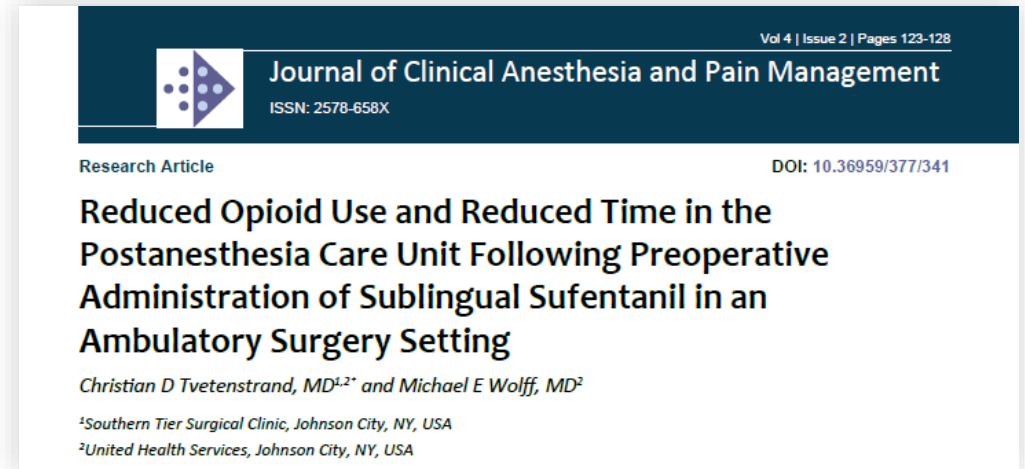
The Department of Defense provided \$22M to develop DSUVIA and approved DSUVIA for all Army SKO's

- The DoD provided \$22M in funding for the development of DSUVIA as the next battlefield analgesic
- The US Army approved DSUVIA for inclusion in all troop's sets, kits and outfits (SKO's), with initial stocking estimated to generated \$30M in revenues over 3 years
- Joint Deployment Formulary approval received in September 2020
- US Army study at UPMC expected to be completed in January 2024



DSUVIA enables opioid stewardship and potentially reduces patient time in the PACU

- Multiple recent studies demonstrating significantly lower amounts of perioperative opioids administered, and reduced patient time in the PACU when DSUVIA was used for analgesia
- When administering DSUVIA there was an overall greater than 50% reduction in opioid equivalents administered, with an 80% reduction in opioids administered post-op in the institution versus the control group.



Q2 2023 financial information/metrics

\$0.3M

Q2 2023 revenues

\$26.3M

Total gross proceeds potential
from July capital raise upon
exercise of all warrants

\$3.8M

Q2 2023 combined R&D
and SG&A⁽²⁾

\$17.4M

Proforma cash and
cash equivalents ⁽¹⁾

(proforma at June 30, 2023)

\$ - M

Senior Debt at
June 30, 2023

\$16-20M

FY 2023 estimated
cash operating expense

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4 Fedsyra™, ephedrine pre-filled syringe NDA submission expected in H2 2023

5 Royalty stream from recently divested commercial product DSUVIA - 15% on commercial sales, 75% on DoD sales and up to \$116.5M in milestones



Thank You

Nasdaq: ACRX