UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

March 13, 2023
Date of Report (Date of earliest event reported)

ARS Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39756**	**81-1489190**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

11682 El Camino Real, Suite 120 **San Diego, California**	**92130**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (858) 771-9307

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	SPRY	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On March 13, 2023, ARS Pharmaceuticals, Inc. (the "Company") updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website and a copy is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated by reference herein.

The information under this Item 7.01 of this Current Report on 8-K, including Exhibit 99.1, is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Company Presentation
104	Cover Page of Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: March 13, 2023

ARS Pharmaceuticals, Inc.

By: /s/ Richard Lowenthal, M.S., MSEL
Name: Richard Lowenthal, M.S., MSEL
Title: President and Chief Executive Officer

Exhibit 99.1

neffy® 2 mg
(epinephrine nasal spray)

THE FIRST NO-NEEDLE, NO-INJECTION SOLUTION for Type I Allergic Reactions

Q1 2023

ARS PHARMA

Forward looking statements

This presentation contains forward-looking statements which include, but are not limited to, statements regarding the design and potential benefits of *neffy*; the anticipated Prescription Drug User Fee Act (PDUFA) date for *neffy*; the timing of regulatory approval for and the commercial launch of *neffy*, if approved; ARS Pharma's commercialization strategy; the potential market opportunity for *neffy*; the projected growth thereof and *neffy*'s ability to capture and grow that market; ARS Pharma's expected competitive position; ARS Pharma's potential to become the standard in treatment and transform the treatment of allergic reactions; the likelihood of *neffy* attaining favorable coverage; the expected intellectual property protection for *neffy*; and any statements of assumptions underlying any of the foregoing. These forward-looking statements are subject to the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. ARS Pharma's expectations and beliefs regarding these matters may not materialize. Actual outcomes and results may differ materially from those contemplated by these forward-looking statements as a result of uncertainties, risks, and changes in circumstances, including but not limited to risks and uncertainties related to: the ability to obtain and maintain regulatory approval for *neffy*; results from clinical trials may not be indicative of results that may be observed in the future; potential safety and other complications from *neffy*; the labelling for *neffy*, if approved; the scope, progress and expansion of developing and commercializing *neffy*; the size and growth of the market therefor and the rate and degree of market acceptance thereof vis-à-vis intramuscular injectable products; the ARS Pharma's ability to protect its intellectual property position; the impact of health epidemics or pandemics on ARS Pharma's business and the actions ARS Pharma may take in response thereto; and the impact of government laws and regulations. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors – Risks Related to ARS Pharma" heading of the company's definitive proxy statement on DEFM14A filed with the Securities and Exchange Commission on October 6, 2022, available at www.sec.gov. These documents can be accessed on ARS Pharma's web page at www.ir.ars-pharma.com by clicking on the link "Financials & Filings."

The forward-looking statements included in this presentation are made only as of the date hereof. ARS Pharma does not assume any obligation and does not intend to update these forward-looking statements, except as required by law.

Potential to Transform the Treatment of Type I Allergic Reactions

- ***neffy®:* first "no needle, no injection" solution** for Type I allergic reactions to address an unmet market need
- **Registration program** demonstrates comparable PK and PD, without risk of needle-related safety concerns, fear and hesitation
- **Significant opportunity to disrupt** current epinephrine injectables market
- **NDA accepted by FDA; mid-2023 PDUFA date anticipated**
- **Potential multi-billion-dollar market** driven by HCP and consumer preference and adoption
- **NCE-like IP exclusivity** potential until at least 2038
- **~$275 million in cash and securities** as of 12/31/2022

Proven leadership team with track record developing and commercializing intranasal and consumer-driven medicines

Richard Lowenthal, M.S.
Chief Executive Officer, Co-Founder
Led FDA approvals for multiple nasal spray products
25+ years of experience

NARCAN® (naloxone HCl) NASAL SPRAY · VALTOCO® (diazepam nasal spray) C · tosymra® (sumatriptan nasal spray) IDmg

Sarina Tanimoto, M.D.
Chief Medical Officer, Co-Founder
Led FDA approvals for multiple nasal spray products
20+ years of experience

NARCAN® (naloxone HCl) NASAL SPRAY · VALTOCO® (diazepam nasal spray) C · tosymra® (sumatriptan nasal spray) IDmg

Eric Karas
Chief Commercial Officer
Led Narcan® commercial ops at Emergent/Adapt, and Auxilium specialty
25+ years of experience

NARCAN® (naloxone HCl) NASAL SPRAY · Testim® (testosterone gel) · XIAFLEX® (collagenase clostridium histolyticum)

Harris Kaplan
EVP, Commercial Strategy
40+ years of commercial strategy across more than 125 product launches

Allegra® · Nexium · VIAGRA®

Dan Relovsky
SVP, Marketing
30+ years of marketing, sales and operational experience across specialty and consumer markets

Brian Dorsey
Chief Operating Officer
25+ years of R&D experience as including multiple head of R&D roles including Pernix, Apricus and Somaxon

Kathy Scott
Chief Financial Officer
30+ years of finance experience with multiple CFO roles including Neurana, Recros and Oncternal

Alex Fitzpatrick
Chief Legal Officer
30+ years of legal experience with multiple GC roles including Evofem, Kyriba, Verenium, Blackbaud

Justin Chakma
Chief Business Officer
10+ years of M&A, licensing, financing and strategy experience including Celgene, Receptos and Auspex

Robert Bell, Ph.D.
Chief Scientific Officer, Co-Founder
30+ years of senior R&D leadership experience including Barr and Somerset

Top-tier board of directors

Pratik Shah, Ph.D.
Chairman of Board of Directors
Executive Chairman at Design, Former Chairman of Synthorx (acq. $2.5B), Former CEO at Auspex (acq. $3.5B)

Richard Lowenthal, M.S.
Chief Executive Officer, Co-Founder
Led FDA approvals for multiple nasal spray products
25+ years of experience

Laura Shawver, Ph.D.
CEO at Capstan, former CEO at Silverback, Synthorx (acq. $2.5B)

Peter Kolchinsky, Ph.D.
Managing Partner and Founder at RA Capital

Brent Saunders
Chairman at The Beauty Health Co., Former CEO of Allergan (acq. $63B), Actavis, Forest Labs, and Bausch + Lomb (acq. $8.7B)

Jonathan Leff
Partner at Deerfield Management
Chairman of Deerfield Institute

Peter Thompson, M.D.
Private Equity Partner at Orbimed

Rajeev Dadoo, Ph.D.
Managing Partner at SR One

Michael Kelly
Former President, US Operations at Adapt (acq. $735M), CEO at Covis (acq. $1.2B), founder at Azur

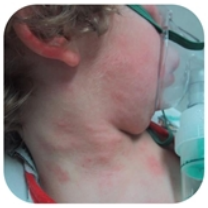
Philip Schneider
Former CFO at IDEC, former Board member at Arena (acq. $6.7B), Auspex (acq. $3.5B), GenProbe (acq. $3.7B)

Saqib Islam, J.D.
CEO of Springworks, former CBO at Moderna and EVP at Alexion

Type I allergic reactions: a life-threatening hypersensitivity reaction

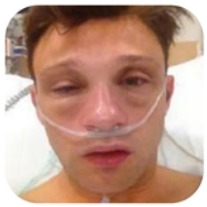
Caused by exposure to a **specific allergen**, most commonly **food**, **venom**, **drugs**

~25 to 40 million people in US with systemic Type I allergic reaction to allergens (e.g., 2+ organ systems involved)



10+ million people with other Type I allergy indications (e.g. urticaria flares, asthma exacerbations)

Significant co-morbidities and symptomatic impact on patient quality of life



More than half a million[1] ER visits each year due to systemic Type I allergic reactions, costing an average of $1600+ per visit[2]

Sources: (1) Carrillo-Martin et al. J Allergy Clin Immunol Pract (2020), (2) BlueCross BlueShield of America. Childhood Allergies in America (2018)
Images Reproduced with permission from Allergy & Anaphylaxis Australia

Epinephrine is effective, but significant device limitations exist

Epinephrine recognized as the **only first-line therapy** by allergy society treatment guidelines[1], but…

- Apprehension to dose due to needle
- Lack of portability
- Reluctance to use in public
- Safety concerns: lacerations, caregiver self-injection, blood vessel hits
- Lack of reliability
- Not user friendly

FDA U.S. FOOD & DRUG ADMINISTRATION

Epinephrine Auto-Injector Devices by Amneal and Impax: CDER Alert - FDA Alerts Patients and Health Care Professionals About Device Malfunction

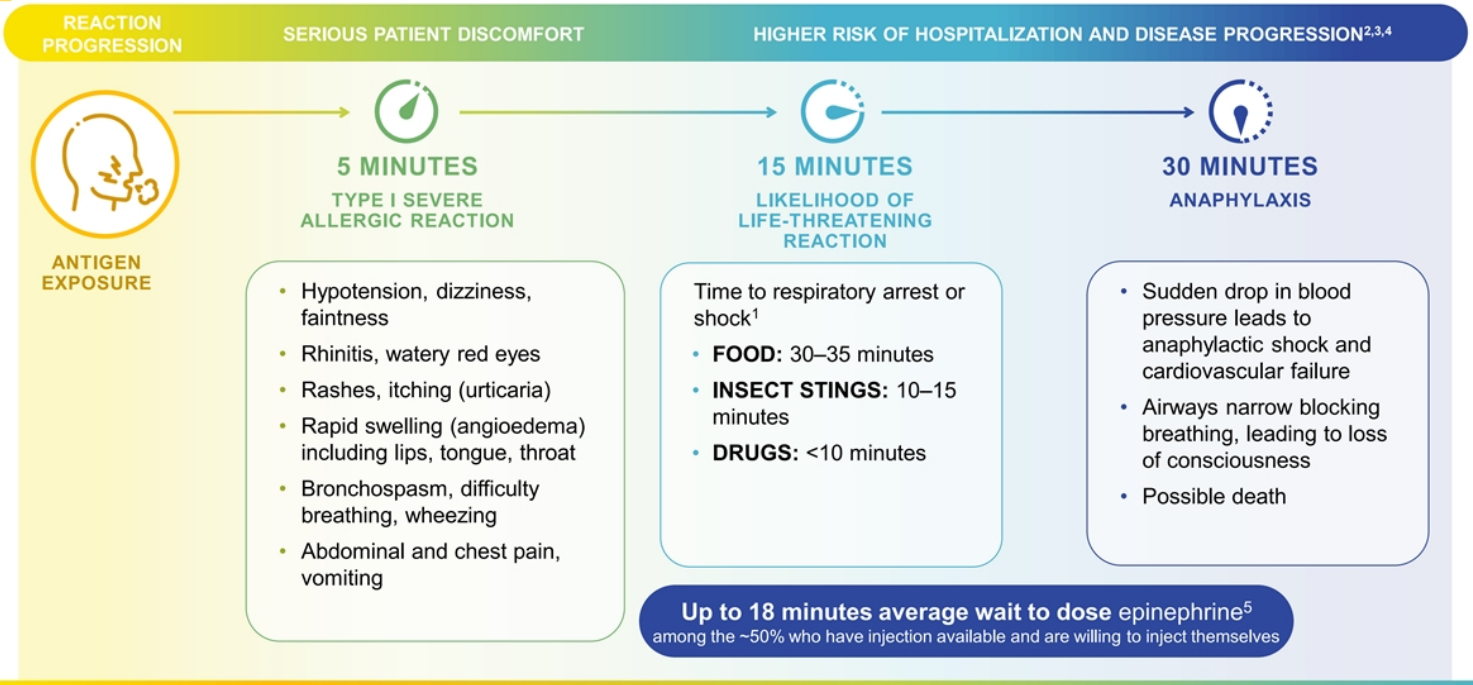
FDA alerts patients and health care professionals of EpiPen auto-injector errors related to device malfunctions and user administration

Bloomberg

7 fatalities and 35 hospitalizations reported due to failures

Sources: [1]Anaphylaxis – a 2020 practice parameter update, systematic review and Grading Recommendations, Assessment, Development and Evaluation (GRADE) analysis

Early intervention with epinephrine is critical in a Type I allergic reaction



Sources: [1] Emergency treatment of anaphylactic reactions: guidelines for healthcare providers. Resuscitation Council (UK); 2016, [2] JF Philips et al. Allergy Asthma Proc (2011), [3] JT Fleming et al. J Allergy Clin Immunol Pract (2014), [4] E. Andrew et al. Prehospital Emergency Care (2018), [5] Data on file from ARS market research

Limitations of injection lead to hesitation and decreased or ineffective usage *neffy* may address these limitations to transform the treatment paradigm

PROBLEM

Only 10% - 20% of Rx filled or used as indicated[6]

NO TREATMENT AVAILABLE	REFUSAL OF TREATMENT	DELAY IN TREATMENT	FAILURE OF TREATMENT
~50% of patients carry[1]	~25% - 50%[1, 3, 5] do not administer	~40 - 60%[2] of patients delay	23 - 35%[4] fail to dose correctly

***neffy®* SOLUTIONS**

1 SMALL

- Fits in your pocket; can carry more than 1
- ~10% of cases require multiple doses of epinephrine[1]

2 NO NEEDLE NO INJECTION

- Rapid administration without a needle
- No risk of needle-related injuries; lacerations[2] or cardiotoxic blood vessel injections
- Less hesitation to dose

3 EASIER AND MORE CONSISTENT DOSING

- 0% critical dosing errors in registration self-administration study
- Low 2 mg dose of epinephrine achieves comparable PK without overexposure risk

4 RELIABLE

- 99.999% delivery of effective dose in reliability testing; no inhalation required
- Same shelf-life as EpiPen, but also stable at high temperatures

Demonstrated PK and PD comparable to injection

Sources: (1) Warren et al. Ann Allergy Asthma Immunol (2018), (2) Data on file from ARS market research, (3) Brooks et al. Ann Allergy Asthma Immunol (2017), (4) El Turki et al. Emerg Med J (2017), (5) Asthma and Allergy Foundation of America Patient Survey Report (2019), (6) Company estimates based on prior references (1) through (5) and IQVIA data

ARS PHARMA

Approved injection products have a range of PK profiles, but are all deemed efficacious (no known difference across products)

TREATMENT	Source	N	Mean Study C_{max} (pg/mL)	Median or Mean Study T_{max} (min)	Study T_{max} range (min)
Epinephrine 0.3 mg IM	Literature	200	209 – 489	30 to 60	3 – 120
	ARS	181	244 – 339	45	4 – 360
Symjepi 0.3 mg	ARS	88	337 – 438	22 to 30	4 – 240
Auvi-Q 0.3 mg*	Literature	67	486	20	5 – 60
EpiPen 0.3 mg	Literature	311	288 – 869	5 – 40	1 – 120
	ARS	196	333 – 753	6 – 24	2 – 240
Total Range			**209 to 869**	**5 to 60**	**1 to 360**

*Baseline corrected

- FDA stated ***neffy*** should be bracketed by PK of approved products
- 0.3 mg IM (needle & syringe) is the reference-listed drug (RLD) and considered to be the gold standard as autoinjectors are a variable mix of IV, SC or IM dosing depending on technique
- All approved products have indistinguishable clinical effect and time to observed clinical benefit: ~90% resolution on first dose within the first 5 to 15 minutes observed for both IM and autoinjectors in literature and practice
- All products approved based on only PK, despite significant PK differences – (i.e. not bioequivalent to each other)
- PD is supportive

neffy clinical program supports NDA filed and accepted by FDA

FDA confirmed three primary registration studies required for ***neffy*** approval

- EPI-15: Single dose and twice dosing in healthy volunteers (n=42)
- EPI-16: Nasal challenge in allergic rhinitis patients (n=36)
- EPI-17: Self-administration in Type I allergy patients (n=42)

IM needle & syringe is the gold standard and reference-listed drug

Primary outcomes for all trials: PK (bioavailability) and PD (SBP, HR)

EPI-10 pediatric trial interim data included in NDA submission, FDA requested

neffy **meets the endpoints discussed with FDA** in completed clinical studies*

Criteria (C_{max}, t_{max}, early partial AUCs) is comparability to epinephrine injection products (bracketed by approved products)

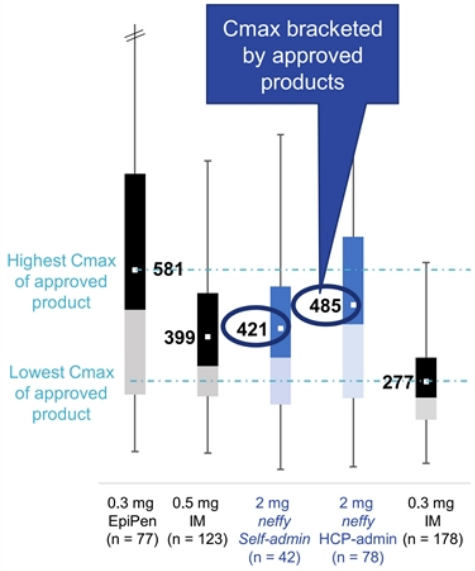
NDA submission accepted by FDA in Q4 2022;
Target PDUFA action date anticipated in mid-2023

Data in subjects aged 4 to 18 (single-arm, non-comparative expected in 2022) to support pediatric labeling
**Pending review by the FDA*

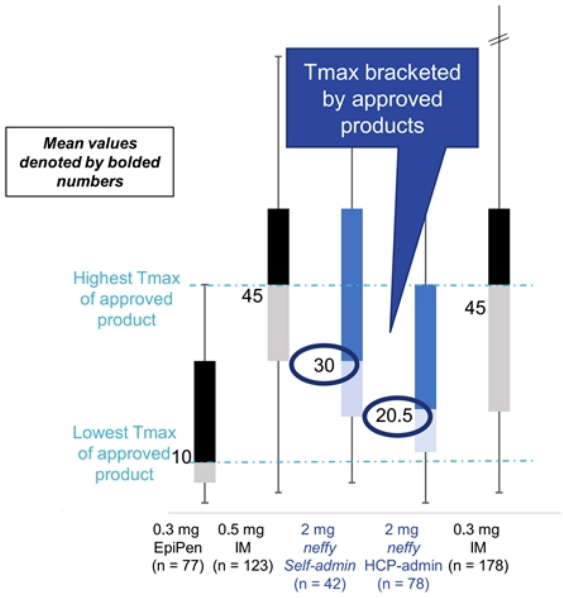
neffy meets FDA-confirmed endpoints in 3 primary studies*

Integrated PK data summary for *neffy* and comparators

Plasma Epinephrine C_{max} (pg/mL)



Median t_{max} (minutes)



Mean Early Partial AUCs

Mean early partial AUCs bracketed by approved products

Treatment	pAUC (0-20)	pAUC (0-45)
0.3 mg IM (n=178)	2,090 (86)	6,290 (61)
2 mg *neffy* (n=78) HCP-admin	**3,610 (84)**	**11,000 (76)**
2 mg *neffy* (n=42) Self-admin	**3,128 (79)**	**11,006 (63)**
0.3 mg EpiPen (n=77)	5,640 (73)	12,000 (53)

Overall mean AUC(0-t) bracketed by approved products

Treatment	AUC_{0-t}
0.5 mg IM (n=123)	43,700 (34)
2 mg *neffy* (n=36)	**37,700 (64)**
0.3 mg IM (n=178)	27,900 (39)

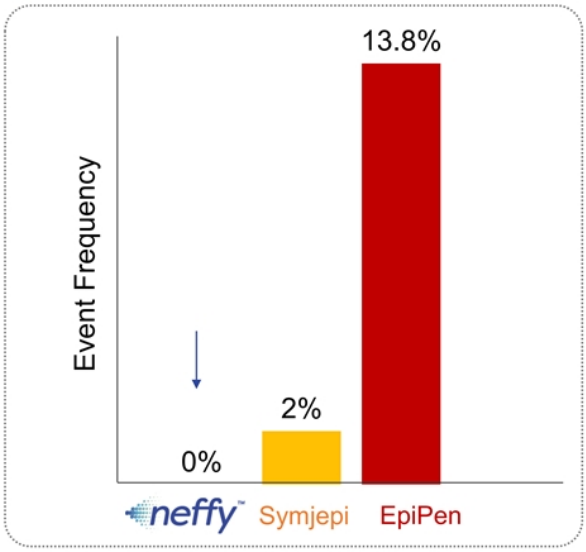
% CV shown in parentheses in tables above

All data from ARS clinical studies
**Pending review by the FDA*

neffy well-tolerated across 600+ individuals dosed in clinical program

- Well-tolerated at all single-doses (0.5 mg to 2 mg) and repeat doses up to 4 mg within 10 minutes
- Mostly grade 1 events and comparable to injection products
- Low Pain Scores: recorded by VAS (100mm scale) with mean scores between 5 and 8 out of a score of 100 across studies
- No irritation based on formal scoring in all studies
- No serious treatment-related adverse events
- No risk of needle-related injuries or blood vessel injections

Risk of blood vessel injection during self-administration that could lead to adverse events

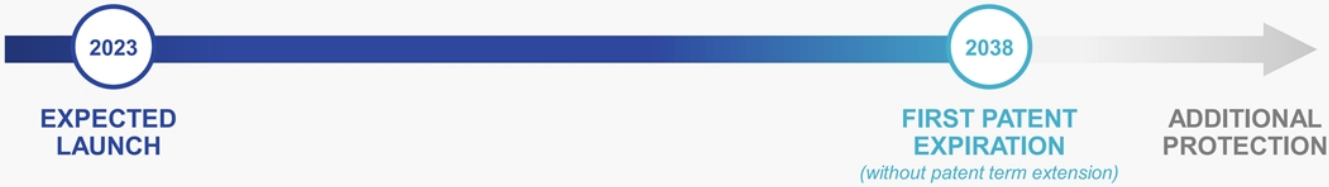


All data from ARS clinical studies

neffy market exclusivity potential until at least 2038

Extensive studies in the lab and clinic completed to develop a proprietary product with expected NCE-like exclusivity

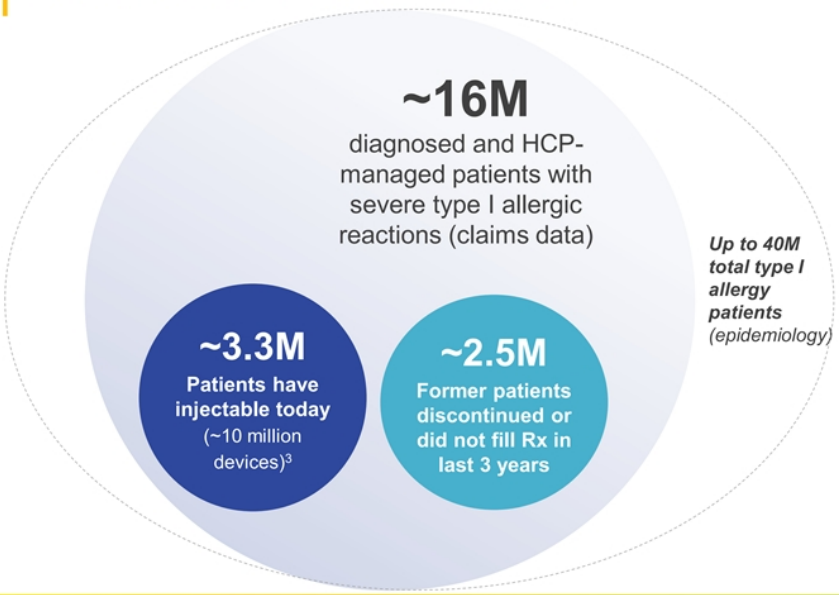
- ✓ **Issued composition of matter patent (US10,576,156) on Intravail® + epinephrine** provides foundational exclusivity blocking any generic products. **Method of treatment patents (US11,173,209; US11,191,838)** block other alkyl glycosides.
- ✓ **Issued method of treatment patent (US10,682,414)** blocks any intranasal epinephrine product using a different technology using a low dose (<2.5 mg)
- ✓ **PCT patent granted in Europe (EP19751807), UK (GB2583051), Japan (JP6941224), Canada (3088909), Australia (AUS2019217643), Korea (10-2375232), China (2019800010042),** with same claims as the US



Commercial Opportunity and Strategy

Significant existing US market opportunity for ***neffy*** penetration

CURRENT ~$1 BILLION[1] ANNUAL EPINEPHRINE MARKET IS THE IMMEDIATE OPPORTUNITY



MULTIPLE LEVERS OF CURRENT MARKET GROWTH

Consistent market growth
+5% y/y in the last ~15 years

Promotional responsiveness
+31% historic lift from Mylan
No meaningful promotion today

More devices per patient
Potential for twice as many ***neffy*** devices annually vs. injectables

[1] SEC filings, IQVIA data and ARS payer research data on file
[2] ARS market research data on file (n = 75 physicians, n = 150 patients), [3] IQVIA extended unit data

Physicians supportive of adopting ***neffy*** into practice

n = 75 Physicians

8.5 out of 10 rating
viewed as a major advance in therapy
10 = MAJOR ADVANCE / **1** = NOT AN ADVANCE AT ALL

100%

Would prescribe *neffy* if their patients asked for it

*No difference in uptake of **neffy** by physician specialty*

neffy addresses the unmet need and is better aligned with what healthcare providers, patients and parents want

n = 150
Current Users

~80% **OF PATIENTS EXPECTED TO SWITCH TO *neffy***

75% **OF NON-FILLING PATIENTS STATED THEY WOULD ASK THEIR PHYSICIAN ABOUT *neffy* RX**

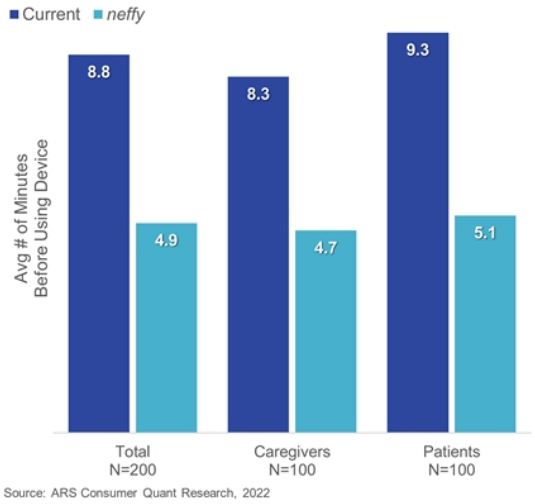
n = 100
Non-fillers

65% to 72%
OF THE TIME,
PEOPLE WHO USE AN OTC WOULD USE ***neffy*** FIRST

69%
OF PEOPLE
WOULD USE ***neffy*** SOONER THAN CURRENT AUTOINJECTOR

Caregivers are enthusiastic about ***neffy*** and its benefits

Time from Onset of Symptoms to Epinephrine Administration



Source: ARS Consumer Quant Research, 2022

> This is fantastic. **Much easier than jabbing the thigh.**
>
> *– Father*

> **I want this. Is it available yet?** Let me know when it is, I will literally call the doctor from my car.
>
> *– Mother*

> We are talking about someone's life and lifestyle here. **Great improvement.**
>
> *– Mother*

> I don't have a co-pay, but I'd get this for my daughters **even if I have to pay $50.**
>
> *– Mother*

Guidelines recommend immediate treatment with epinephrine. Earlier administration is associated with improved clinical outcomes and decreased likelihood of hospitalizations.

By Addressing Needle Injector Deficiencies
neffy can Become the Standard in Treatment

Propensity of Current SAR Patients Prescribed a Needle Injector

Don't Use Properly[1]

Don't Keep On Hand[2]

Delay Treatment[3]

neffy Patient Research Shows…

45% ↑
Faster Treatment Time[3]

47% ↑
More Likely to Fill Rx[3]

Would Keep On Hand[3]

Used Device Correctly[4]

(1) ARS Consumer Quant Research, 2022, (2) Warren et al. Ann Allergy Asthma Immunol (2018), (3) Data on file from ARS market research, (4) ARS human factors studies

Payer research supports positive reimbursement environment

Key findings from discussions with ~50 decision-makers within the major payers and PBMs:

- Category is generally not restricted, unlike biologics and orphan disease drugs with high WACs
- Payers view ***neffy*** as a valuable and differentiated treatment option
- High likelihood of attaining favorable coverage (Tier 2 or 3) for ~80% of lives

*"This is a **game-changer**; it really addresses the unmet needs we currently have in this space, specifically the safety and tolerability issues."*
– Payer

"Nasal delivery will overcome some negative perceived factors of an injection."
– Payer

*"If this is priced properly, this could be a '**state-of-the-art therapy**' for patients."*
– PBM

"There is no value in delaying access to a product like this and nothing to prior authorize (PA). We can't PA if the patient needs it."
– PBM

Commercial strategy and imperatives

From needle to neffy:

- Convert the existing market
- Bring back patients that are lapsed
- Bring in patients who should be carrying epinephrine now, but do not carry

1. Ensure broad and rapid ***neffy*** coverage as well as affordable access for patients
2. Change HCP habits and switch prescribing from needle to ***neffy***
3. Drive ***neffy*** awareness and new patient growth (into and back into) the market

Strategic Imperatives and CSFs: From Needle to ***neffy***

	1	2	3
STRATEGIC IMPERATIVES	**Ensure broad and rapid *neffy* coverage as well as affordable access for patients**	**Change HCP habits and switch prescribing from needle to *neffy***	**Drive *neffy* awareness and new patient growth (into and back into) the market**
CRITICAL SUCCESS FACTORS	• Payers recognize the value proposition of ***neffy*** • Patients can access ***neffy*** • Prescriptions are filled seamlessly	• HCP awareness at launch • Confidence in ***neffy*** and intranasal delivery • Allergists and KOL endorsement	• Consumer awareness of ***neffy*** • Patient understanding of effectiveness and safety • Patients will ask for ***neffy*** proactively

Integrated HCP Promotion to Drive Awareness and Reach with Current Epinephrine Prescribers Representing >40% of Prescriptions*

Specialty Salesforce

Virtual Salesforce

Non-Personal Promotion

FTEs	**~125 FTEs**	**Top 50,000** *Decile 5 to 10*
HCP Reach	**~ 15,000 HCPs**	

HCP promotion will be supported by DTC promotion to drive expansion within the addressable SAR market

** Reaching >80% of Prescriptions from Allergists, ENTs, and Pediatricians*

neffy is positioned potentially to transform the treatment of serious allergic reactions

PK superior to IM (Reference listed drug & gold standard)
offers therapeutic exposures and makes it easy to switch

Effective

No meaningful side effects
No needle-related injuries possible

Safe

No serious safety risks associated with injection devices (needle)
No blood vessel injections, no lacerations, no bone injections

No Needle

Less Hesitation to Dose

No needle, no fear, no wait
Easier to use and more reliable delivery than with autoinjectors (less chance of failed dosing)

Compact

Always available
with child, parent and caregiver

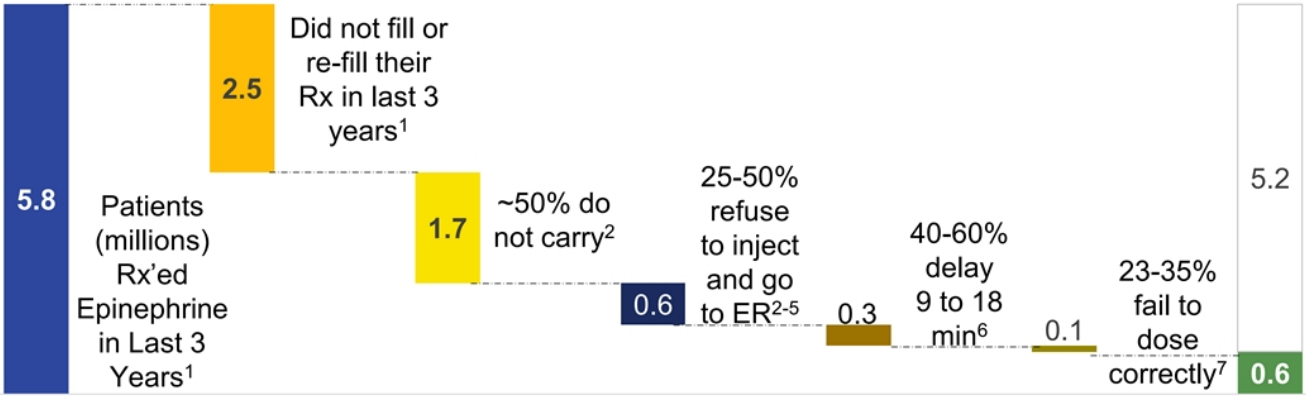
Easy to Use

100% of adults (N=105) successfully dosed
in human factors studies

Supplemental Slides

Many patients/caregivers do not administer treatment or delay use during reaction

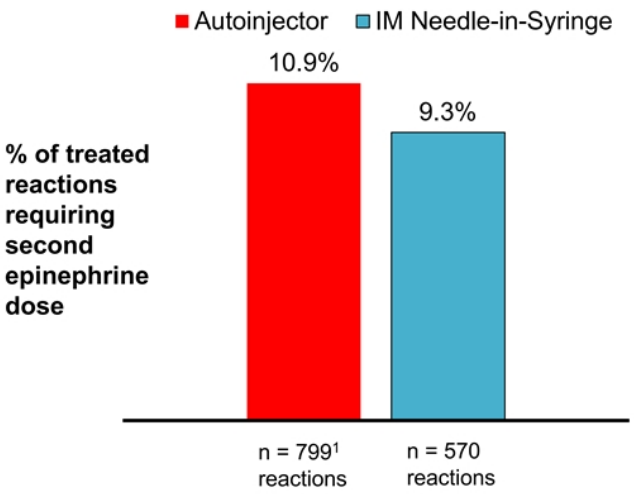
Approx. 40,000,000 people with serious Type I Allergic Reactions
~5,800,000 people received Rx from a Physician in Last 3 Years



~10%-20% of patients receiving Rx treat as indicated (~2% of overall population)

1. IQVIA Claims Data 2022, 2. Warren 2018, 3. Brooks 2018, 4. Asthma and Allergy Foundation of America 2019 ,
5. Casale 2022, 6. ARS data presented at AAAAI 2023, 7. El Turki 2017

IM Needle & Syringe is the Historical Product Clinically Proven to Be Effective: No Difference in Efficacy Between IM and EAIs



- Meta-analysis of 88 studies with 36,557 anaphylaxis events w/ epinephrine use in 50.4% of events (approx. 10% repeat dose needed)
- 12 major studies with 100% autoinjector (80+% EpiPen[1]) or 100% IM-needle-and-syringe use in community or ED setting.[2]
- Need for repeat dose is approximately 10% with EpiPen or IM (despite PK differences)[2]
- More rapid PK does not appear to provide clinical benefit, but does add risk (e.g. IV bolus injection of epinephrine is well known to be unsafe)

1. 79.6% of the autoinjector treated reactions are specifically identified occurring with EpiPen, 2. Patel J Allergy Clin Immunol (2021)

History of FDA Approved Community Use Products

- No observed clinical differences between autoinjectors and IM injection (time to onset or efficacy)

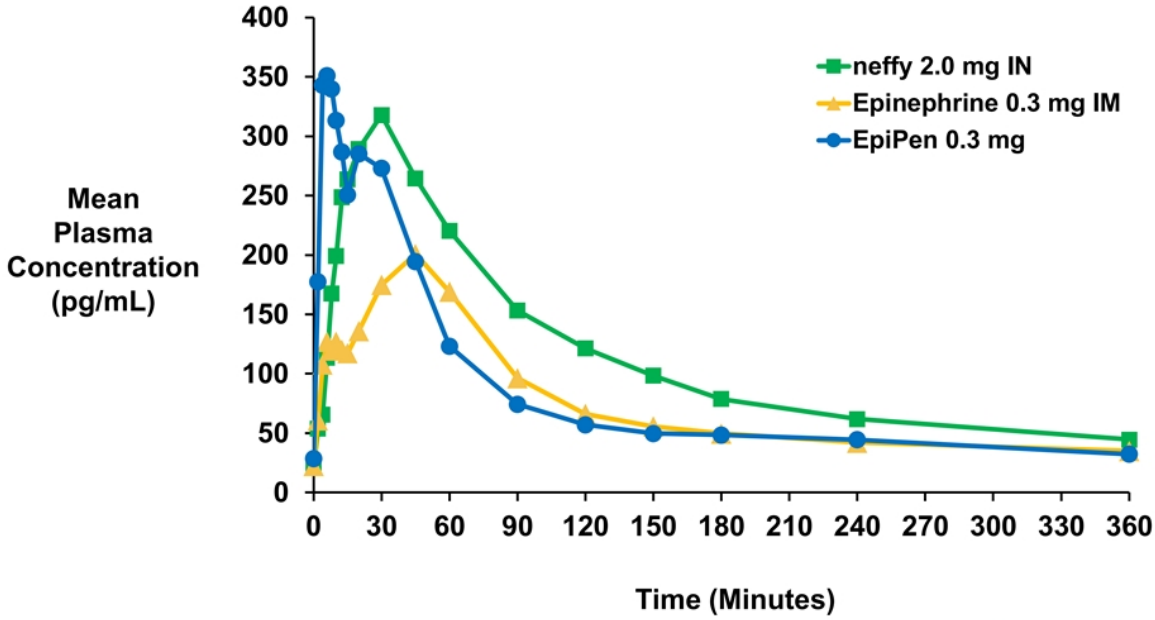
Device (Approved)	Approval Basis	Pharmacokinetics (any data including literature)
EpiPen (1987)	No PK Data	Significant differences (EpiPen vs. IM) only known in past ~10 yrs Significant blood vessel injection risk (IV bolus) only known last 5 yrs
Twinject (2003)	No PK Data	No PK data known to date
Adrenaclick (2003)	No PK Data	No PK data known to date
Auvi-Q (2012)	Single PK Study vs. EpiPen	More rapid PK vs. IM, but **slower PK vs. EpiPen** (t_{max} = 20 min vs. 10 min)
Symjepi (2017)	No PK Data	ARS studies show **slower PK vs. *neffy* or other autoinjectors**
Teva Generic Epipen (2018)	No PK Data	None to date; shorter needle and different activation force

neffy Development Approach Agreed with FDA

- ***neffy*** should demonstrate primary PK parameters C_{max}, t_{max} and $pAUC_{0-20/0-45}$ within the range of injection products
  - AUC_{0-t} was secondary for safety only
- IM injection (needle and syringe) is RLD for efficacy; EpiPen is the upper limit for safety (maximum exposure safe enough for use)
- PD outcomes are supportive (should be at least as good as injection)

Bracketing Criteria	Lower Bracket	Upper Bracket
C_{max} (primary)	0.3 mg IM	0.3 mg EpiPen
t_{max} (primary)	0.3 mg IM	0.3 mg EpiPen
$pAUC_{0-20,\ 0-30,\ 0-45}$ (primary)	0.3 mg IM	0.3 mg EpiPen
AUC_{0-t} (secondary)		0.5 mg IM

Integrated Results ***neffy*** 2 mg Studies (EPI 15 & EPI 16)



neffy 2 mg Single Dose Bracketed by Injection

Product	N	Mean C_{max} (pg/mL) (CV%)	Median T_{max} (minutes) (range)	$pAUC_{0-20}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-45}$ (min*pg/mL) Mean (CV%)	AUC_{0-t} (min*pg/mL) Mean
Epi 0.3 mg IM	**178**	**277 (65)**	**45 (4-360)**	**2090 (86)**	**6290 (61)**	**27900 (39)**
Symjepi 0.3 mg	36	438 (65)	30 (4-90)	3560 (82)	10400 (56)	23700 (38)
***neffy* 2 mg (self-administration)**	**42**	**421 (66)**	**30 (6-240)**	**2964 (71)**	**10545 (63)**	**46776 (56)**
***neffy* 2 mg**	**78**	**485 (71)**	**20.5 (2-150)**	**3610 (84)**	**11000 (76)**	**40900 (68)**
EpiPen 0.3 mg	**77**	**581 (76)**	**10 (2-45)**	**5640 (73)**	**12000 (53)**	**31600 (39)**

neffy PK is Also Bracketed by EpiPen Studies

Treatment	Study Reference	N	Mean Study C_{max} (pg/mL)	Median Study T_{max} (min)	T_{max} range (min)	Administration
EpiPen (0.3 mg)	AQST-109 EPIPHAST II Results (2022)	22	869	22	5 to 40	HCP
EpiPen (0.3 mg)	ARS EPI-JP01 Data (2020)	30	676	10	2 to 45	HCP
EpiPen (0.3 mg)	ARS EPI-15 (2022)	35	612	8	2 to 45	HCP
EpiPen (0.3 mg)	Tal et al. EAACI (2022)	12	550	9	n.d.	HCP
EpiPen (0.3 mg)	ARS EPI-11b Data (2021)	9	537	6	2 to 6	HCP
EpiPen (0.3 mg)	Edwards et al. NDA #201739 (2012)	67	520	10.2	4 to 60	HCP
EpiPen (0.3 mg)	Chen et al. AAAAI (2019)	11	511	5	3 to 50	HCP
EpiPen (0.3 mg)	ARS EPI-12 Data (2021)	36	493	8	3 to 154	Self-Admin
EpiPen (0.3 mg)	ARS EPI-13 Data (2022)	39	490	6	2 to 240	Self-Admin
neffy (2.0 mg)	ARS EPI-16 data (2022)	36	491	20	2 to 120	HCP
***neffy* (2.0 mg)**	**ARS integrated analysis (2022)**	**78**	**485**	**20.5**	**2 to 150**	**HCP**
neffy (2.0 mg)	ARS EPI-15 data (2022)	42	481	30	6 to 150	HCP
neffy (2.0 mg)	ARS EPI-17 data (2022)	42	421	30	6 to 240	Self-Admin
EpiPen (0.3 mg)	Worm et al. Clin Transl Allergy (2020)[2]	12	390 to 530	9 to 30	3 to 120	HCP
EpiPen (0.3 mg)	Turner et al. Clin Exp Allergy (2021)[3]	37	386	40	3 to 90	HCP
EpiPen (0.3 mg)	Amphastar US2021/030502 (2021)[1]	56	364 - 458	7 - 15	n.d.	HCP
EpiPen (0.3 mg)	ARS EPI-07 Data (2019)	35	375	24	4 to 45	HCP
EpiPen (0.3 mg)	Dworaczyk et al. AAAAI (2020)[1]	55	308 to 440	10 - 16	1 to 61	HCP
EpiPen (0.3 mg)	Oppenheimer et al. AAAAI (2022)	10	341	22	5 to 90	HCP
EpiPen (0.3 mg)	ARS EPI-01 Data (2018)	12	333	20	6 to 45	HCP
EpiPen (0.3 mg)	Aquestive R&D Day (2021)	9	300	10[4]	n.d.	HCP
EpiPen (0.3 mg)	Dworaczyk et al. AAAAI (2021)	25	288	10	5 to 90	HCP

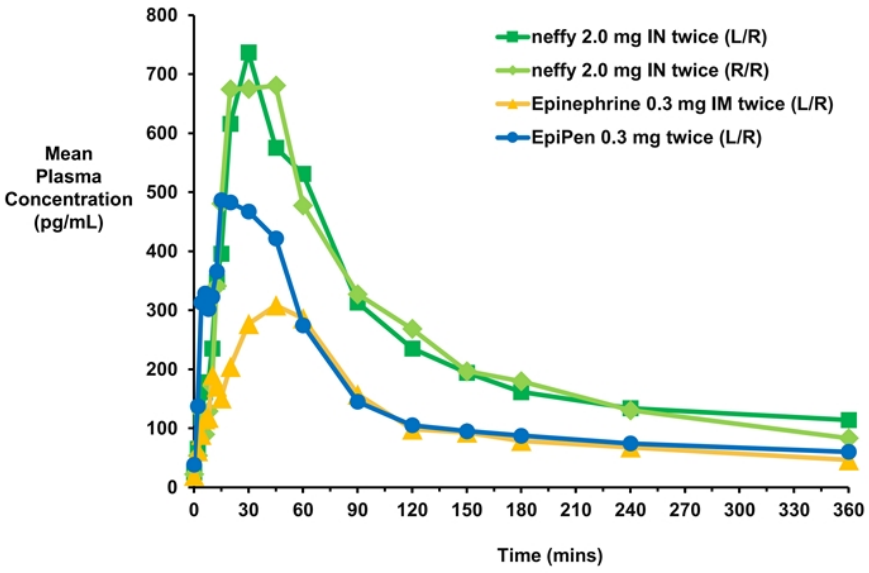
1. 2 cohorts; 2. 5 cohorts; 3. Data from publication and cited approval dossier from the Lakemedelsverket Medical Products Agency, 4. Mean tmax value only

Pediatric *neffy* Pharmacokinetics (EPI-10 Interim Analysis)

Product	N	Mean C_{max} (pg/mL) (CV%)	Median T_{max} (minutes) (range)	$pAUC_{0-20}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-45}$ (min*pg/mL) Mean (CV%)	AUC_{0-t} (min*pg/mL) Mean
***neffy* (1.0 mg) Children 30 kg+**	26	253 (66)	20 (7.5-120)	2,570 (78)	5,960 (52)	14,000 (53)
***neffy* (2.0 mg) Children 30 kg+**	16	540 (71)	25 (2.5-120)	4,140 (78)	13,500 (76)	35,500 (76)
***neffy* (2.0 mg) Adults (Integrated)**	78	485 (71)	20.5 (2-150)	3,610 (84)	11,000 (76)	40,900 (68)

- Larger children (30+ kg) have similar but slightly higher exposures as compared to adults with 2 mg
- Proportional results between 1 mg and 2 mg doses in 30+ kg group
- Data supported by Pharmacologically Base Absorption Model (PBAM) and POP PK

neffy 2 mg Twice Dosing – Two Doses 10 Minutes Apart

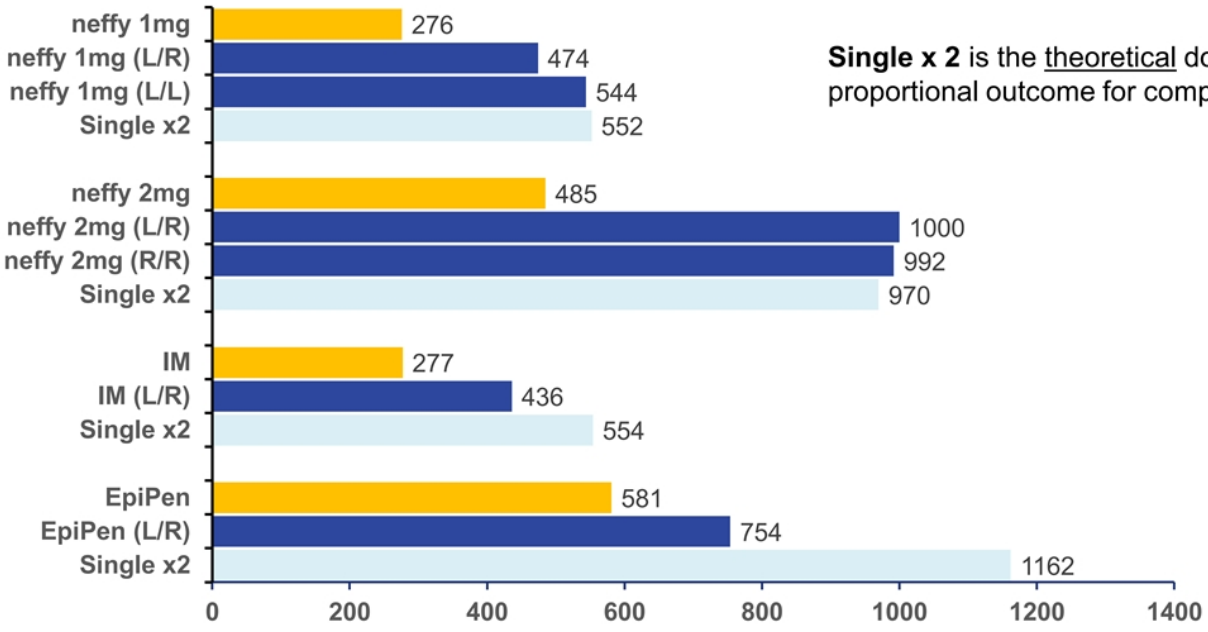


Treatment	N	Mean C_{max} (pg/mL) (%CV)	Median t_{max} (min) (range)
neffy 2.0 mg twice (L/R)	39	1000 (93)	30 (6 - 150)
neffy 2.0 mg twice (R/R)	39	992 (75)	30 (4 - 150)
Epinephrine 0.3 mg IM twice (L/R)	70	436 (49)	45 (6 - 180)
EpiPen 0.3 mg twice (L/R)	78	754 (65)	20 (4 - 360)

Benchmark concentrations at 20 min:

neffy 4 mg twice (R/R):	616 pg/mL
neffy 4 mg twice (L/R):	675 pg/mL
Epi 0.3 mg IM twice:	204 pg/mL
EpiPen 0.3 mg twice:	483 pg/mL

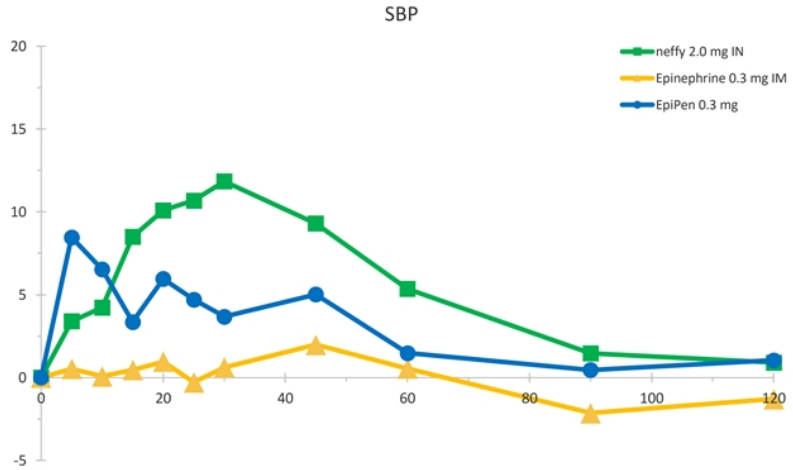
neffy integrated PK is dose-proportional based on mean Cmax

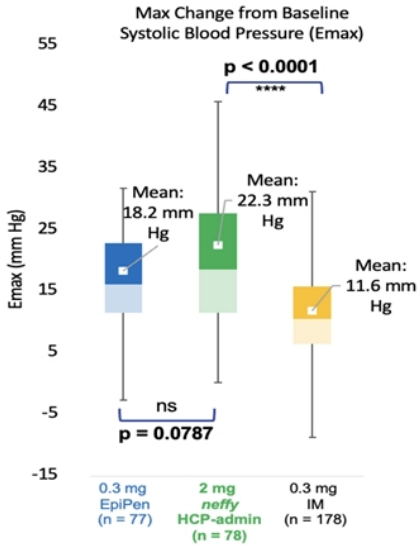


Single x 2 is the theoretical dose proportional outcome for comparison

Mean SBP Response from a Single ***neffy*** 2 mg is Comparable to or Better than Injection Products

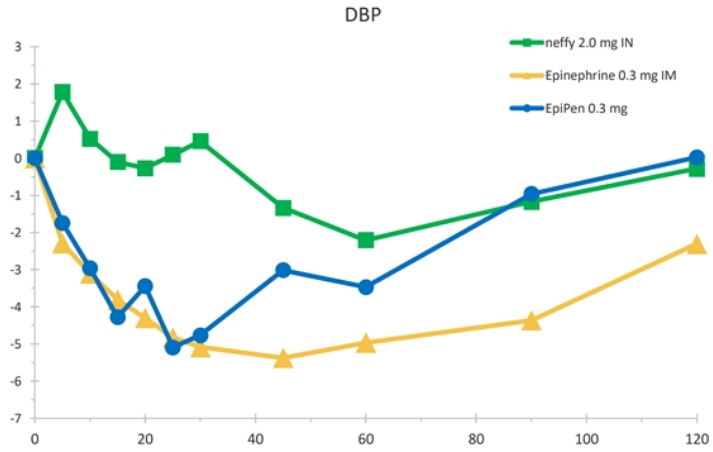
- SBP response from intranasal administration is more consistent with mean effect greater than injection products

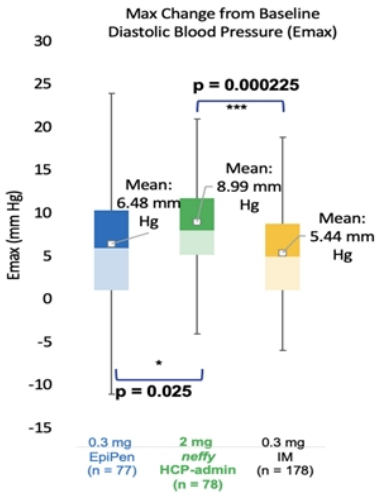




Mean DBP Change for a Single 2 mg ***neffy*** Demonstrates Less Early Decrease than Injection Products

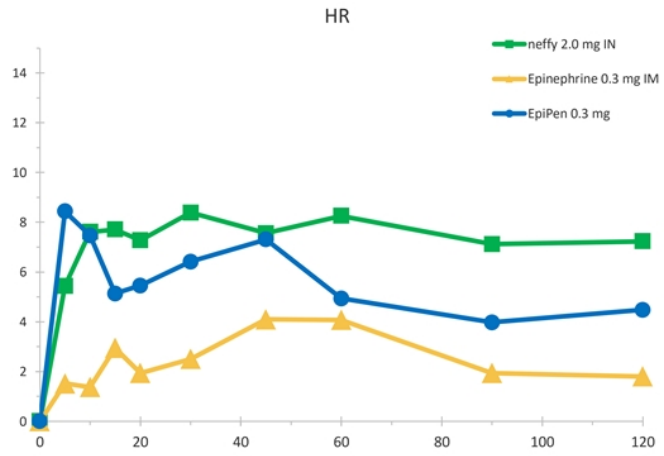
- Initial greater decrease in DBP after IM administration suppresses SBP and is not desirable in patients with hypotension. Direct to systemic routes of administration result in less decrease in DBP.

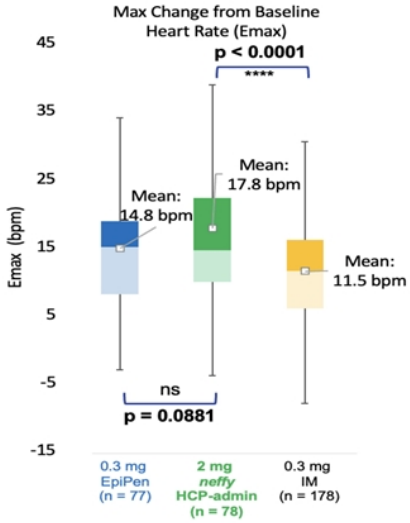




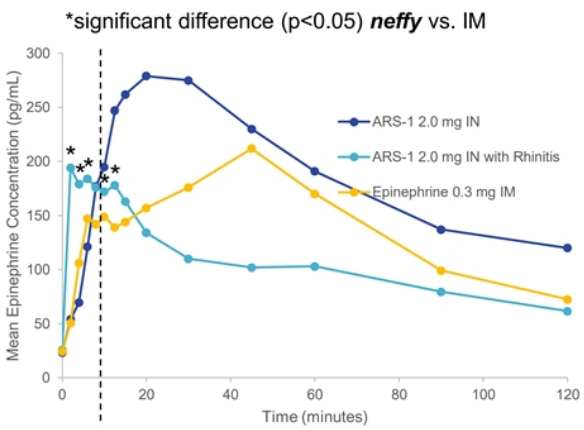
Mean HR Response from a Single 2 mg ***neffy*** is Comparable to or Better than Injection Products

- HR response from intranasal administration is more consistent with mean effect greater than injection products





neffy PK greater than 0.3 mg IM during Nasal Allergen Challenge (Worse Case Nasal Condition: EPI-16 study)



10 min median time to re-dose per guidelines (5-15 min)

Treatment	N	t_{max} (min) median (range)	C_{max} (pg/mL)	AUC_{last} (min*pg/mL)
			mean (%CV)	mean (%CV)
***neffy* 2.0 mg**	36	20 (2-120)	491 (65)	37100 (66)
***neffy* 2.0 mg with rhinitis**	34	7 (2 – 90)	303 (68)	23300 (69)
Epi IM 0.3 mg	35	45 (4– 360)	259 (62)	26000 (42)

Results:

- Edema (congestion) results in more rapid absorption compared to normal nasal conditions
- Rhinorrhea may cause more rapid drainage, so drug is cleared more quickly (lower Cmax and AUC compared to normal nasal conditions)
- Cmax greater and tmax more rapid than IM 0.3 mg injection

neffy Early Partial Exposures greater than 0.3 mg IM injection after Nasal Allergen Challenge Rhinitis Induction (EPI-16 study)

Product	N	$pAUC_{0-10}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-15}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-20}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-30}$ (min*pg/mL) Mean (CV%)	$pAUC_{0-45}$ (min*pg/mL) Mean
Epi 0.3 mg IM normal	35	966 (80)	1610 (78)	2280 (80)	3790 (77)	6430 (70)
***neffy* 2 mg rhinitis**	**34**	**1610 (58)***	**2460 (59)***	**3200 (66)***	**4400 (71)***	**5970 (73)**
***neffy* 2 mg normal**	36	1060 (93)	2270 (84)*	3630 (79)*	6400 (67)*	10200 (62)*

*significant difference ($p<0.05$) between ***neffy*** w/ NAC rhinitis and IM

- Absolute concentration higher for ***neffy*** with NAC induced rhinitis through 15 mins
  - 10 min: 172 pg/mL vs. 149 pg/mL (***neffy*** w/ Rhinitis vs. IM)
  - 15 min: 163 pg/mL vs. 144 pg/mL (***neffy*** w/ Rhinitis vs. IM)
  - 20 min: 133 pg/mL vs. 157 pg/mL (***neffy*** w/ Rhinitis vs. IM)
- Treatment guidelines indicate repeat dose in 5-15 minutes if no response

Conclusion: ***neffy*** with NAC induced rhinitis gives higher exposures compared to IM through clinically relevant period prior to second dose administration