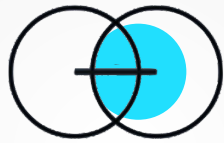
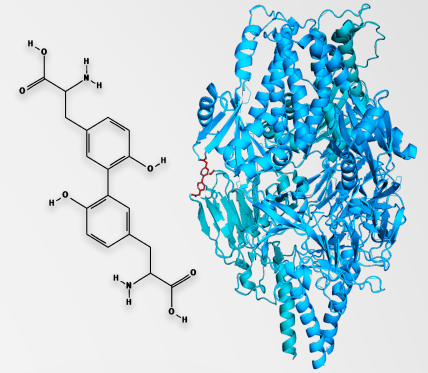




# ENGINEERING LIFE: Shaping the Future of Vaccines ■

# OVERVIEW



## BEST-IN-CLASS VACCINE PLATFORM

Next generation fusion protein vaccines



## RSV IND BY END OF 2024

Lead RSV vaccine at clinical manufacturing stage



## RAISING \$8M TO IND

Clinical manufacturing, Tox, to IND



VRC/NIAD



SBIR-STTR



NIH NIAID



NEW YORK STATE OF OPPORTUNITY  
Empire State Development



NIH National Institute on Aging



INDIE BIO



SUSV



McLellan Lab  
TEXAS  
The University of Texas at Austin



ENDLESS FRONTIER LABS

biodextris



iavi

BioBAT



DOWNSTATE HEALTH SCIENCES UNIVERSITY



UNIVERSITY OF FLORIDA



Crowe Lab

# BLOCKBUSTER TRENDS

Vaccines have emerged as a growing class of blockbuster candidates



**Vaccines #2 category of top 50 pharmaceuticals in 2022.**

COVID \$90B, Gardasil \$7B. Prevnar \$6B, Shingrix 4B.



**2030 sales projected to approach \$250B.**

CAGR of 25%.



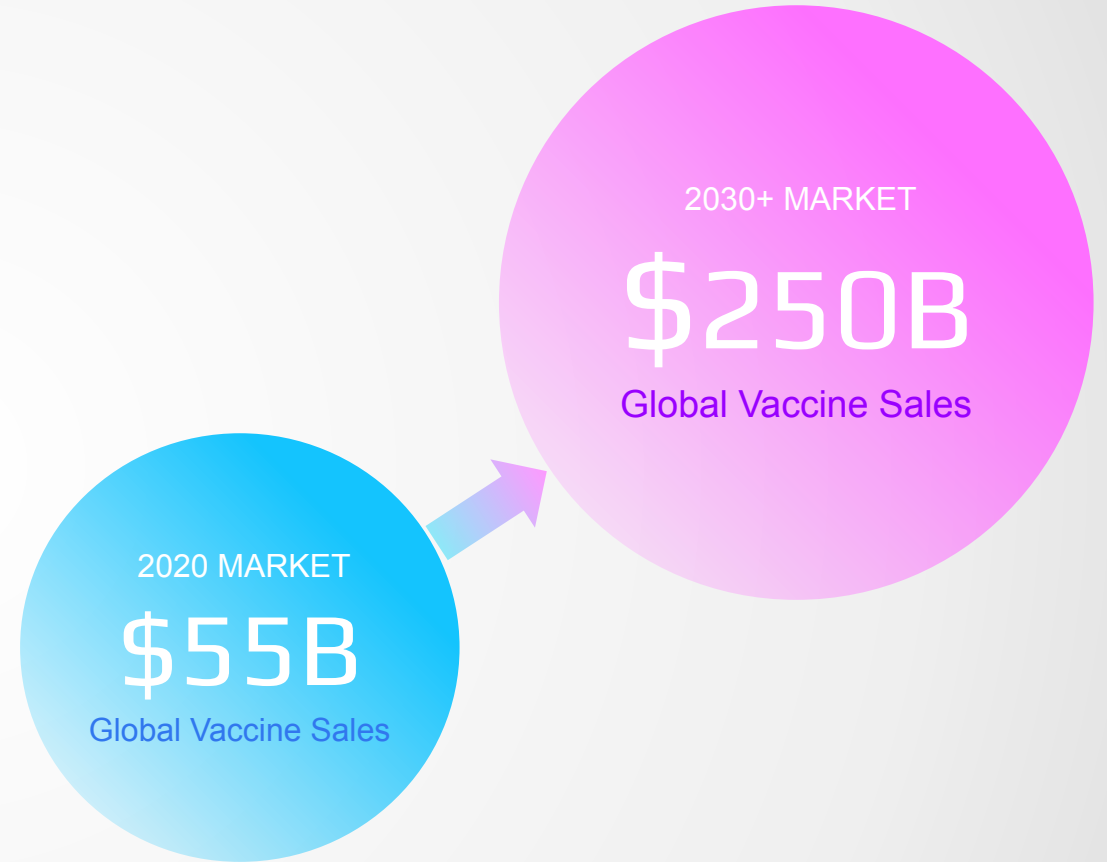
**Vaccine pricing unaffected by Inflation Reduction Act.**

Vaccine pricing increasing substantially since *before* pandemic. New RSV vaccines highest vaccine per-dose price ever.



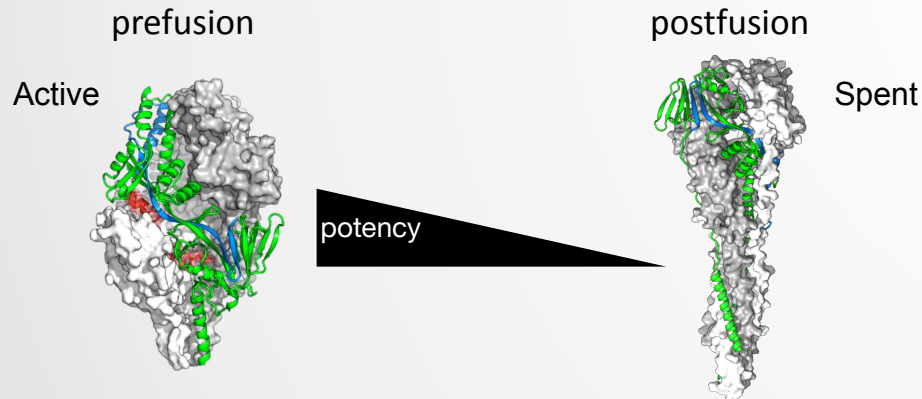
**Post-pandemic shortened reg pathway for vaccines.**

Post-pandemic, shortened development pathway for vaccines, particularly short for next-gen vaccines

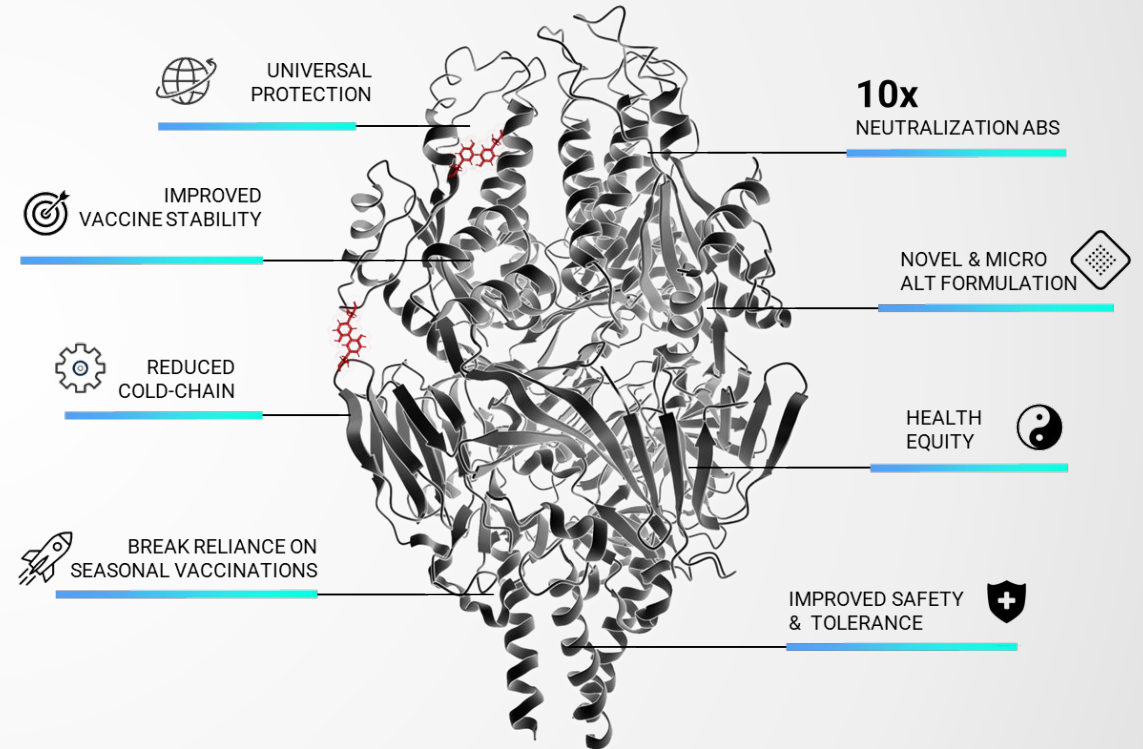


# BEST-IN-CLASS POTENTIAL

- Widely accepted & hugely successful protein subunit approach
- Important viral vaccine immunogens: conformationally unstable. Max potency e.g. in "prefusion"
- Calder's **3D-Vaxlock™** platform targets "molecular staples" to lock in vaccines' most potent 3D shape



Calder's 3D-Vaxlock™ technology yields most stable, most protective, and safest viral protein-based vaccines

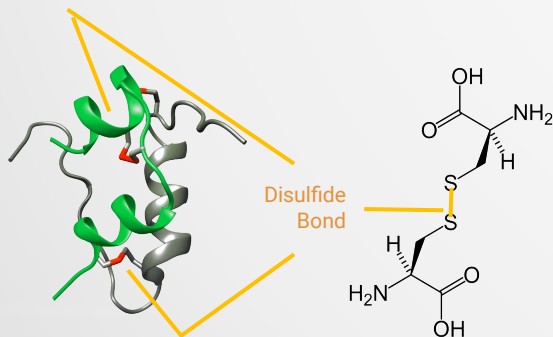
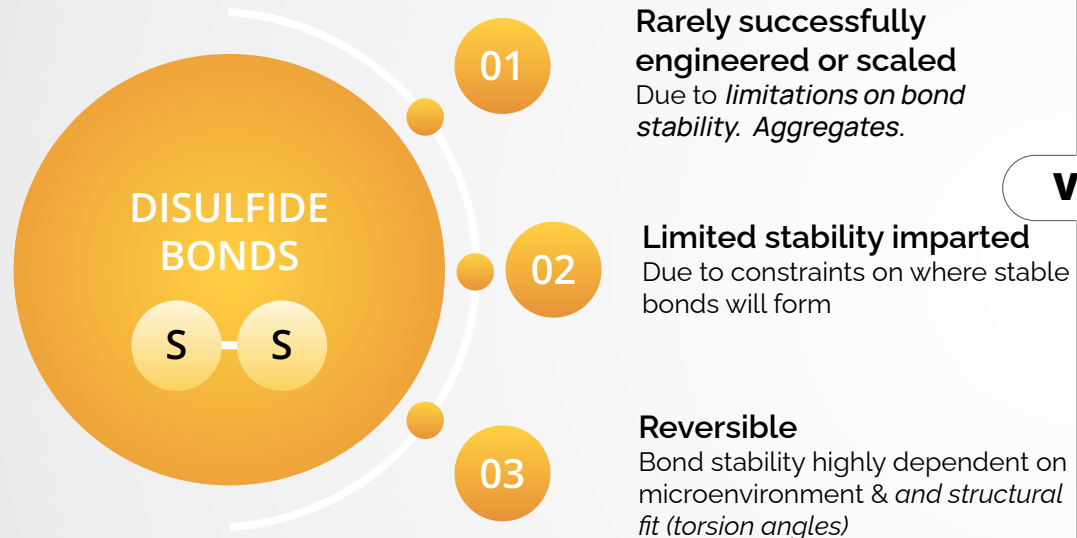


**3D-Vaxlock™** combines structure-based design & bioprocess, generates novel composition of matter IP

# TARGETED DITYROSINE

Targeted dityrosine engineering delivers on the promise of covalent bonding between natural amino acids

## Conventional



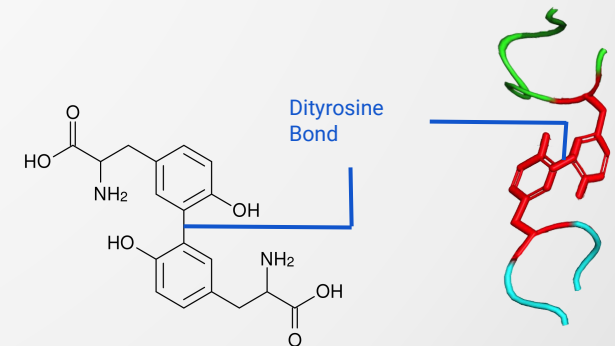
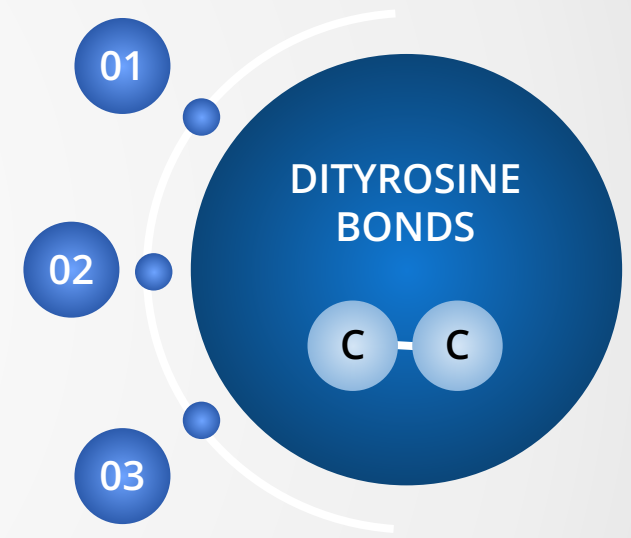
**VS**

## Calder's "Molecular Staples"

**Clear engineering**  
*Form between Tyr side-chains in structural proximity. Slot-in technology*

**High stability imparted**  
Impressive degree of stability imparted; limitations still being explored

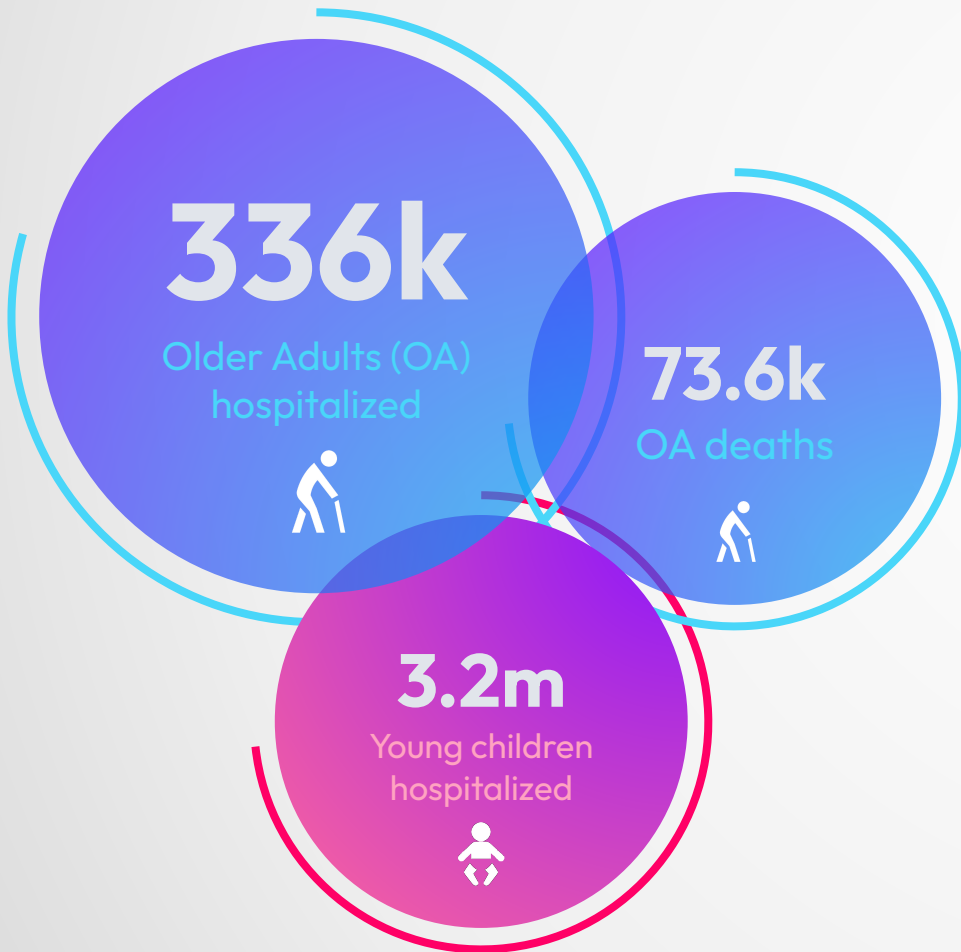
**Irreversible**  
Tyr phenolic rings form physiologically unbreakable **C-C bond**



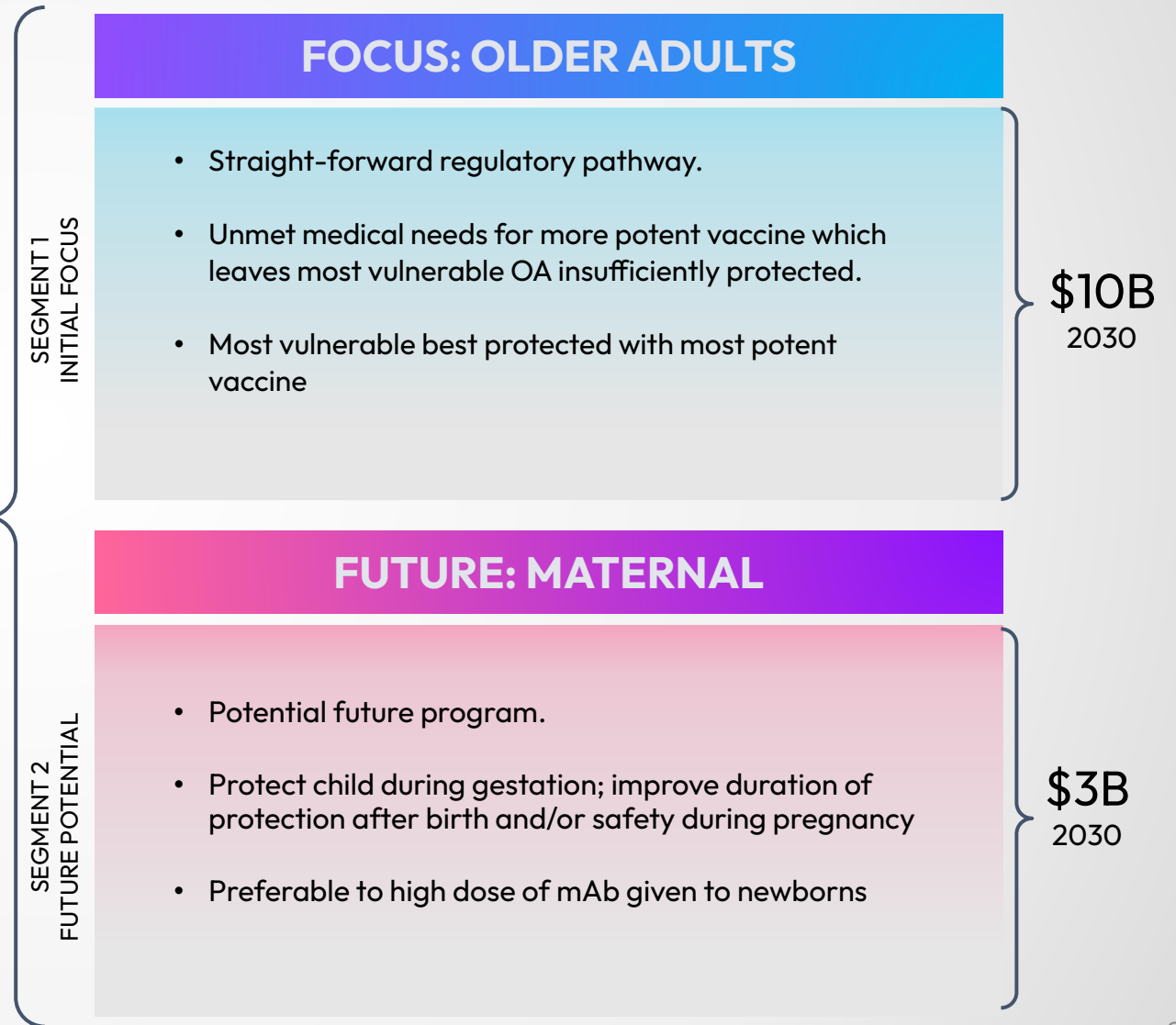
# LEAD PROGRAM – RSV VACCINE

RSV F in its prefusion conformation by far the most potent and best RSV vaccine immunogen for older adults (OA)

## RSV DISEASE BURDEN



**\$13B**  
Market Opportunity



# preF BEST RSV IMMUNOGEN

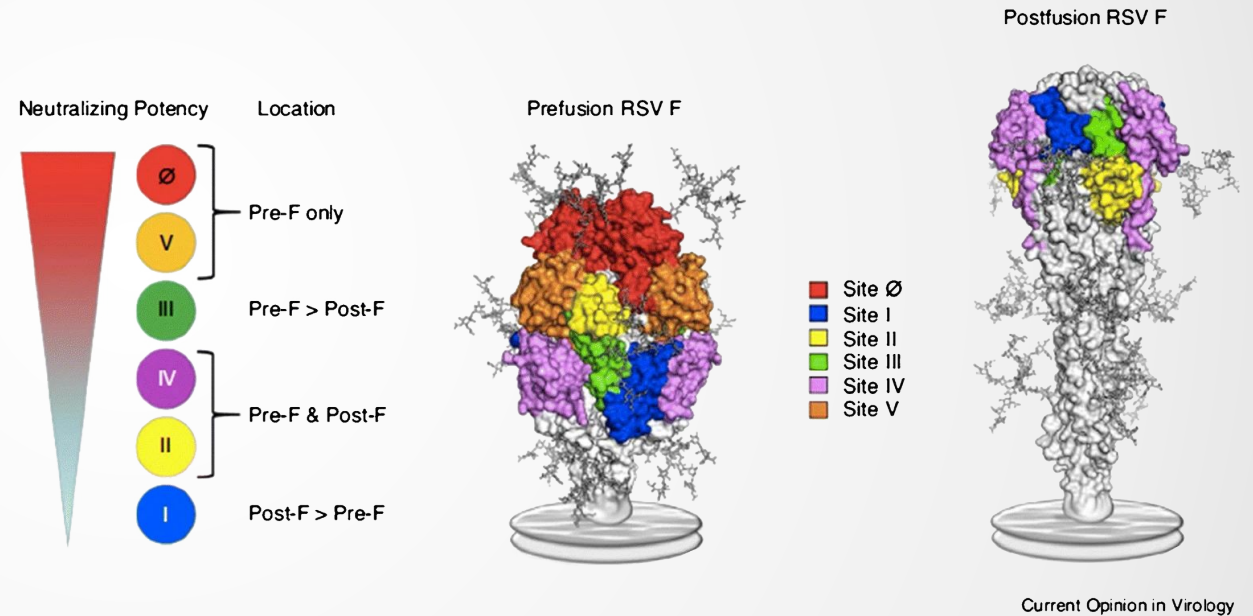
RSV F in its prefusion conformation by far the most potent RSV vaccine immunogen

## RSV F by far the best RSV vaccine immunogen

RSV F elicits the strongest neutralizing Abs that protection broadly against RSV A & B

- RSVF is a viral surface protein that mediates viral entry – the first step in infection
  - Antibodies to F in its active, “prefusion” conformation prevent infection.
- F is highly conserved
  - Antibodies to F recognize, bind, and neutralize all strains of RSV A & B

## For max potency, RSV F must be in prefusion conformation

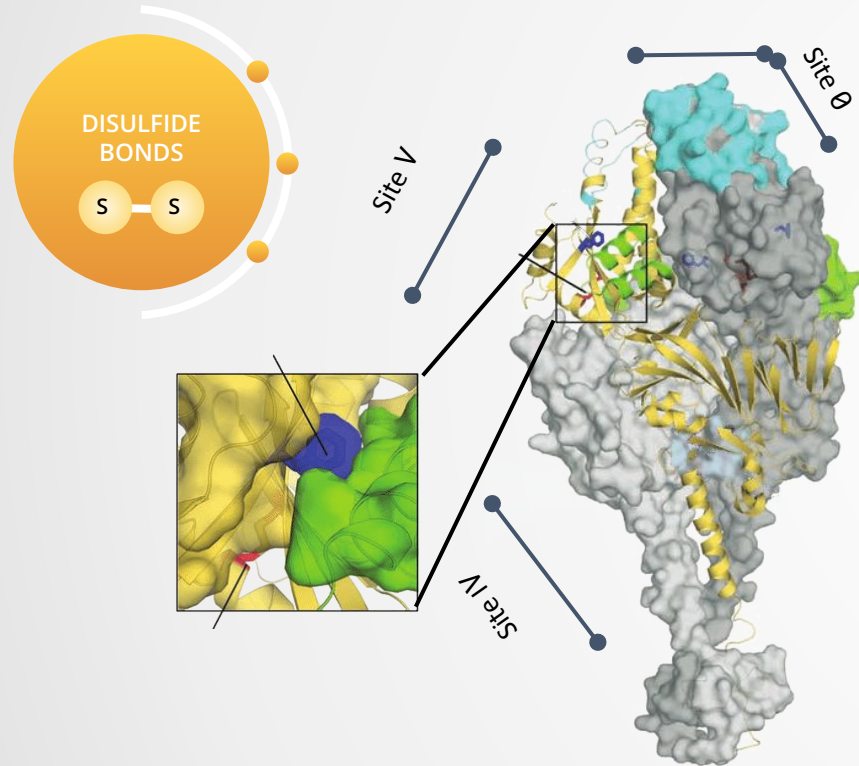


Conformational instability of RSV preF was barrier to vaccine development

# CLD-001: VaxLock preF

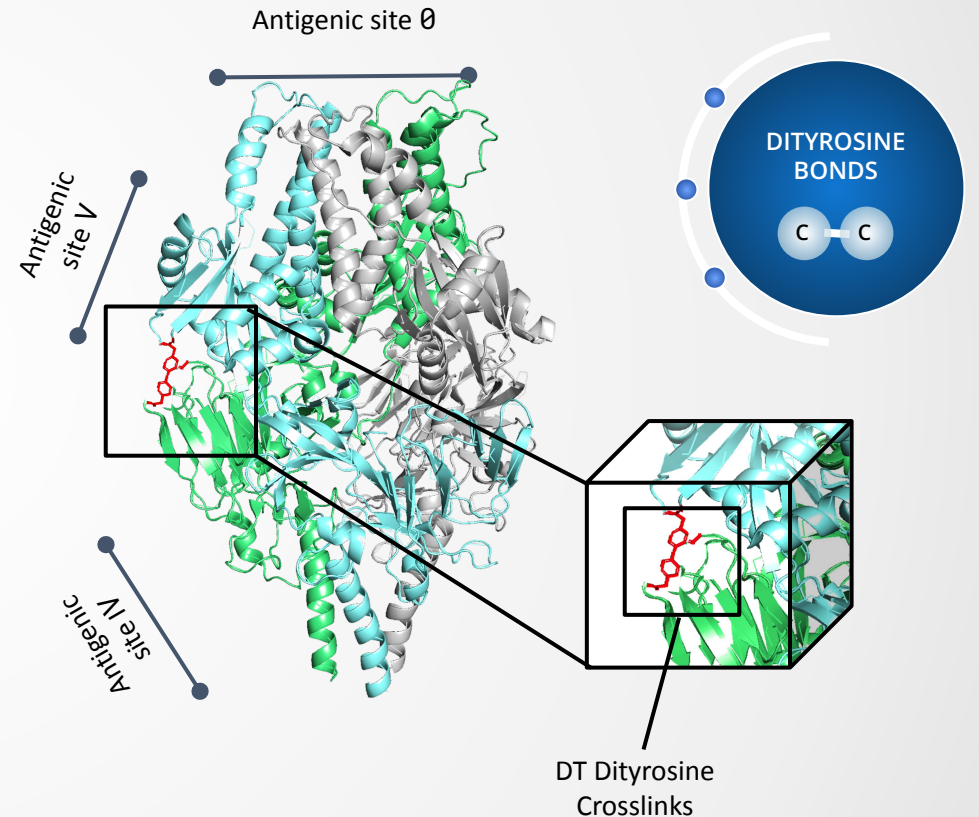
Nano-scale, site-specific dityrosine (DT) crosslinking technology creates best-in-class stabilized subunit vaccines

Conventional  
POC: DS-Cav1 (NIH)\*



VS

Calder's "Molecular Staples"  
Calder's CLD-001



First-gen: Arexvy (GSK) & Abrysvo (PFE): modified DS-Cav1 immunogens

Disulfide bonds enabled 10X higher neutralizing antibodies vs postfusion

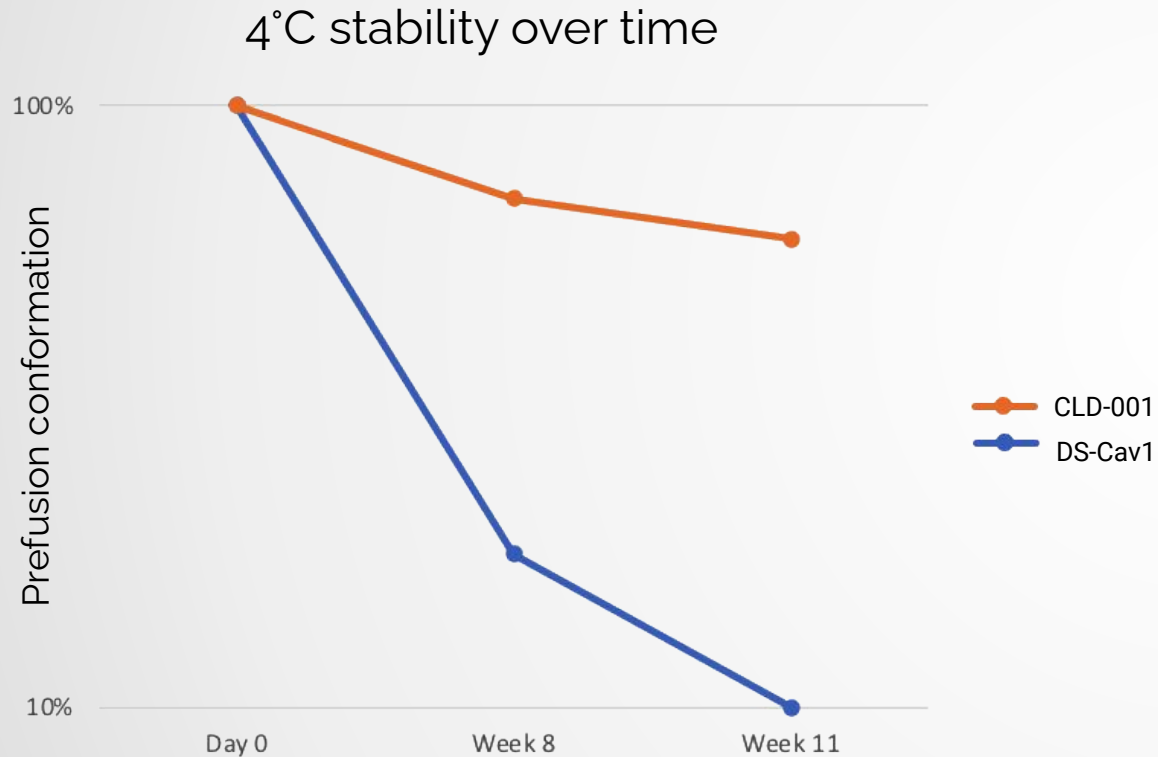
CLD-001 elicits 11.1X higher neutralizing antibodies vs DS-Cav1

\*McLellan et al. 2013. Structure-based design of a fusion glycoprotein vaccine for respiratory syncytial virus. doi: 10.1126/science.1243283.



# STABILITY

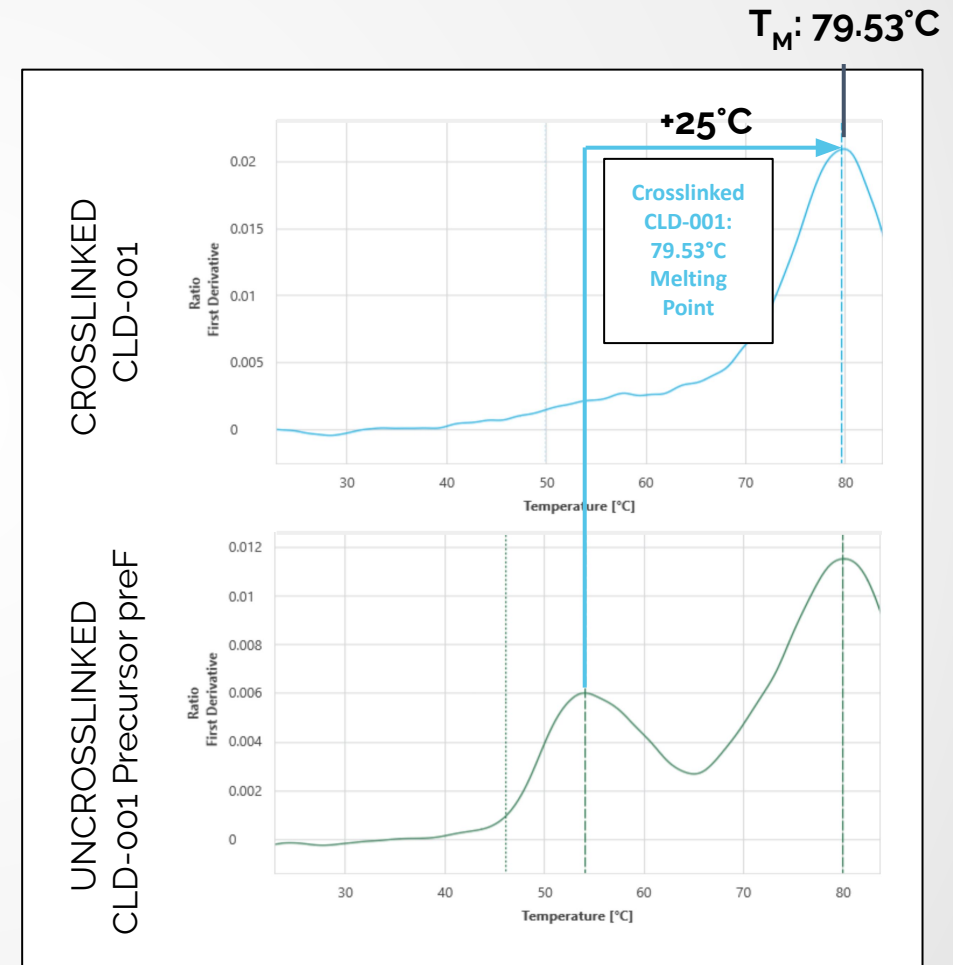
Best-In-Class  
Conformational Stability\*



\*Prefusion antigenicity measured with sandwich ELISA using two perfusion-specific mAbs: 5C4 + AM14

Prolonged/enhanced B cell signals to conformational neutralizing epitopes of CLD-001 - far better neut Ab titers, avidity & memory

Best-In-Class  
Thermostability\*\*



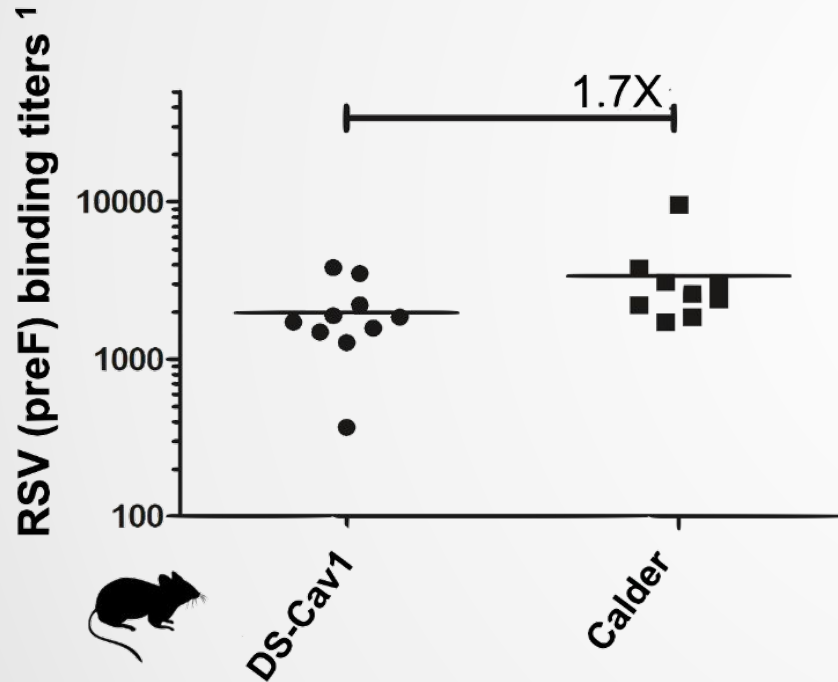
\*\*Melting temperatures before and after crosslinking measured by differential scanning fluorimetry (DSF)

# CLD-001: MOST POTENT RSV preF VACCINE

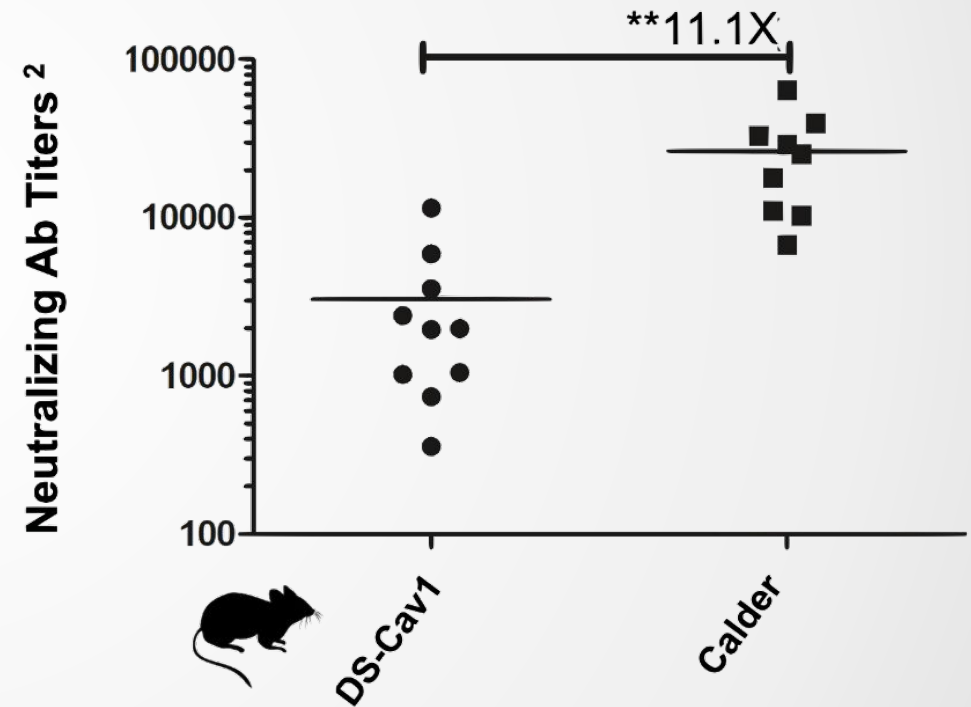
In mice, CLD-001 elicits very high-quality responses with 11-fold higher neutralizing antibody titers

**Greater potency provides more effective and longer-term protection**

Calder's vaccine elicits greater Ab responses



..and much higher neutralizing Ab responses



**Highest-quality responses improve efficacy but also reduce side-effects**

<sup>1</sup> OD<sub>450</sub> readings; <sup>2</sup> 50% inhibitory concentration (IC<sub>50</sub>) of antibodies in serum that neutralize the ability of RSV to infect

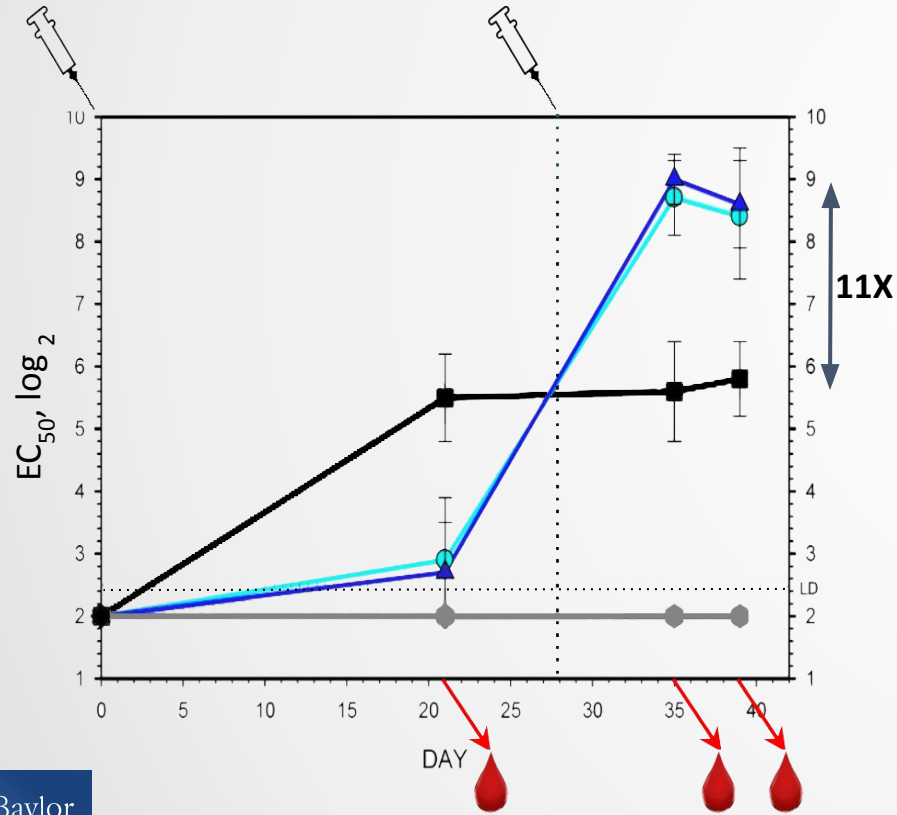
# EFFECTIVE PROTECTION

In gold-standard cotton rat model, CLD-001 elicits high nAb titers and fully protects from viral challenge

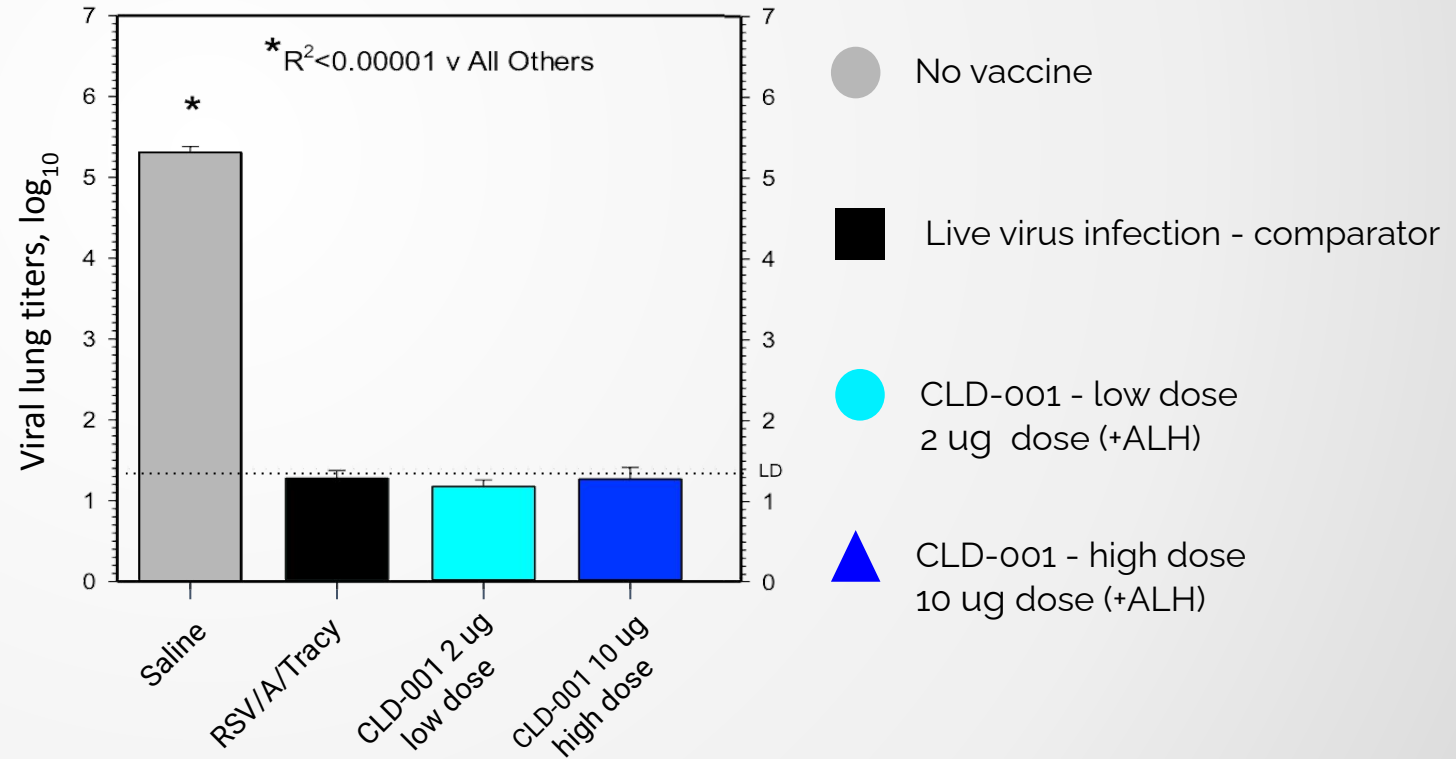
With cotton rat results, Calder's RSV vaccine is ready for clinical development



RSV A Neutralizing Ab Titers

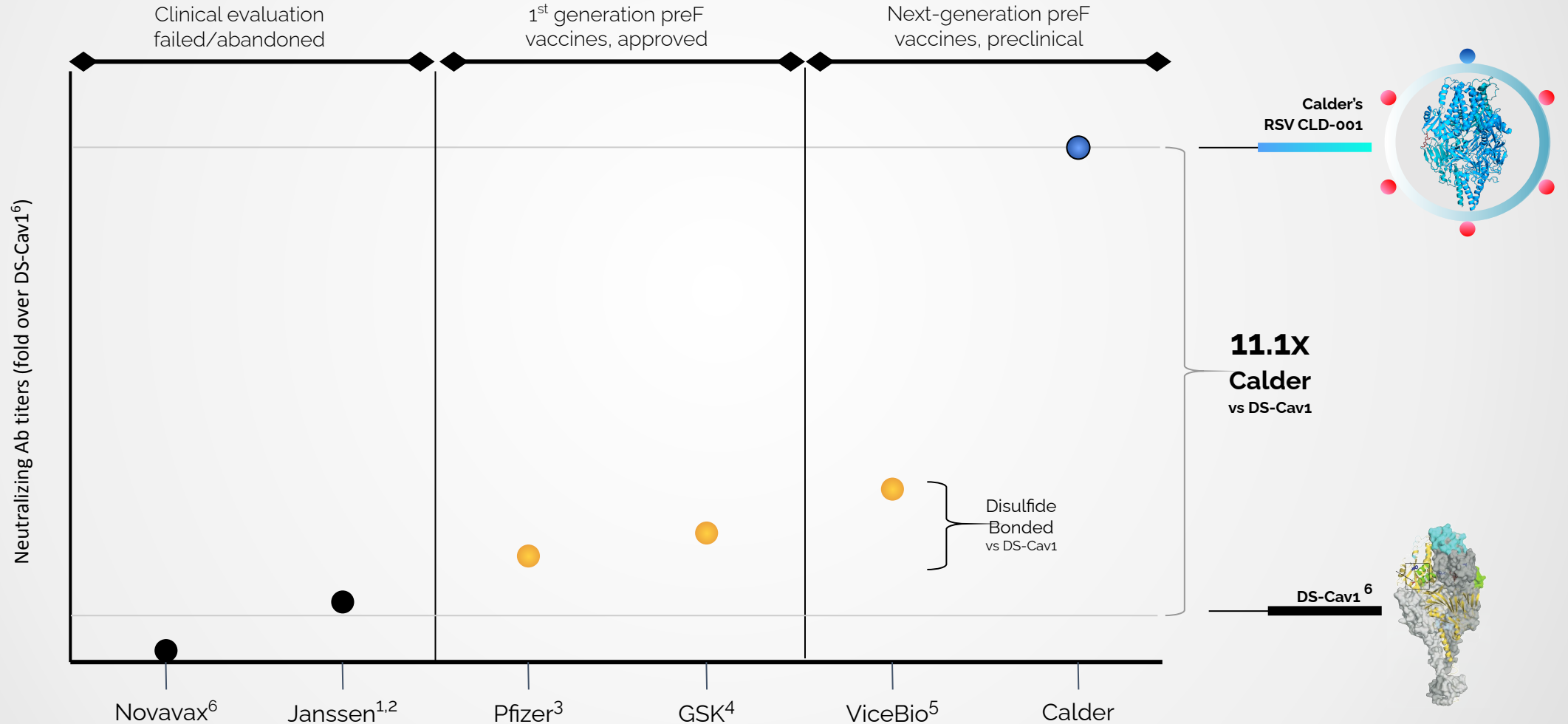


RSV A Viral Lung Titers



# preF SUBUNIT POTENCY

RSV neutralizing antibody titers *best correlate of protection*.  
CLD-001 will best protect the vulnerable



<sup>1</sup> Krarup et al., 2015; <sup>2</sup> protein+adenovector; <sup>3</sup> US 9,950,058; <sup>4</sup> bovine titers from US 17/262,098; <sup>5</sup> US 11,254,712; <sup>6</sup> McLellan et al., 2013. DS-Cav1 = industry standard



# RSV-HISTORIC EVIDENCE

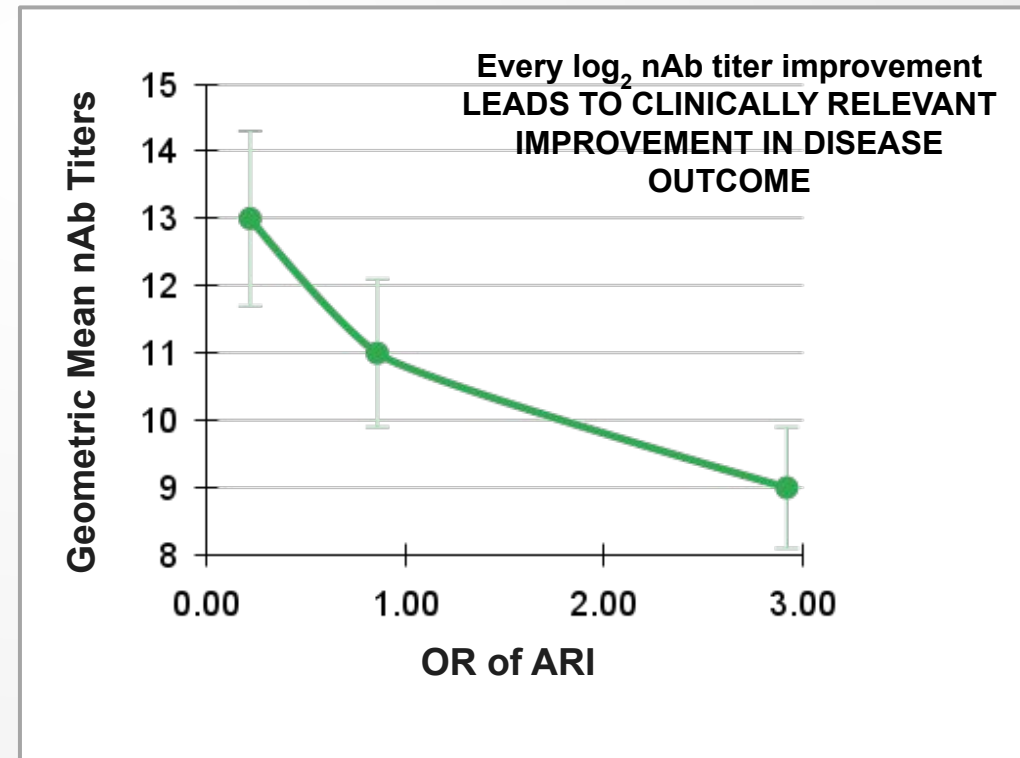
Neutralizing antibody titers best correlate of protection

## Highest neutralizing antibody titers key to best RSV protection

Increase in neutralization titers highly correlated with decrease in RSV Acute Respiratory Infection (ARI) odds ratio (OR)

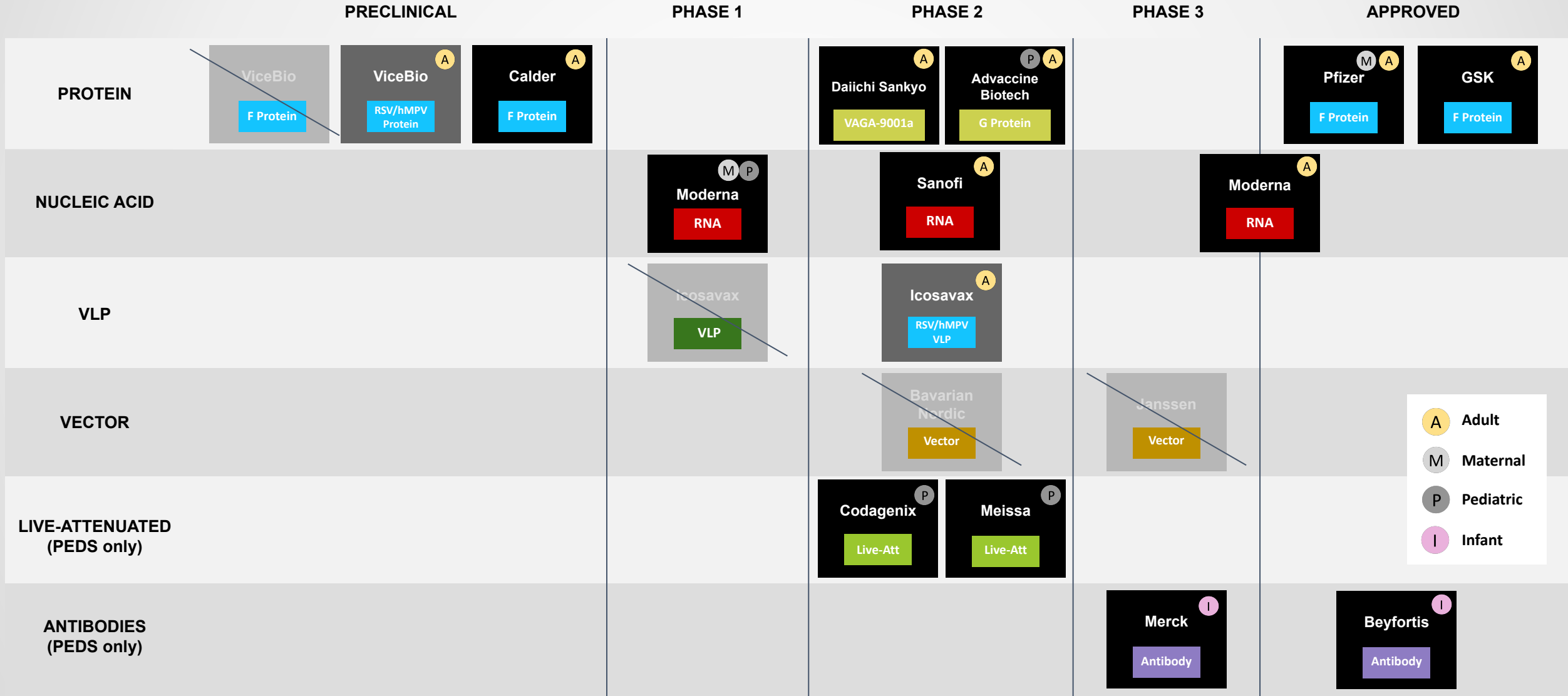
GROUP	GEOMETRIC MEAN NAB TITERS	OR OF ARI (ODDS RATIO OF ARI)
1	13.0+	0.22
2	11.1 - 12.0	0.86
3	< 9.01	2.92

Phase 2 Sanofi study of a postfusion RSV vaccine in high risk elderly; followed subjects for 2 years and tracked RSV infection (PCR)  
Falsey, ResViNet, Malaga 2017 (adapted); Falsey et al 2008, J Infect Dis; Walsh et al 2004; Falsey et al 2010



# COMPETITION THINNING OUT

RSV neutralizing antibody titers best correlate of protection.  
CLD-001 best-in-class next generation protein vaccine



# CLD - 001 ADVANTAGES



**Stability** CLD-001 is the most stable protein immunogen.  
Highest melting point: 79.53°C.



**Neutralizing Abs** CLD-001 achieves neutralizing antibody titers 4x Arexvy (GSK), 5x Abrysvo (PFE) & 11.1x DS-Cav1.  
Neutralizing ab titers best correlate of protection.



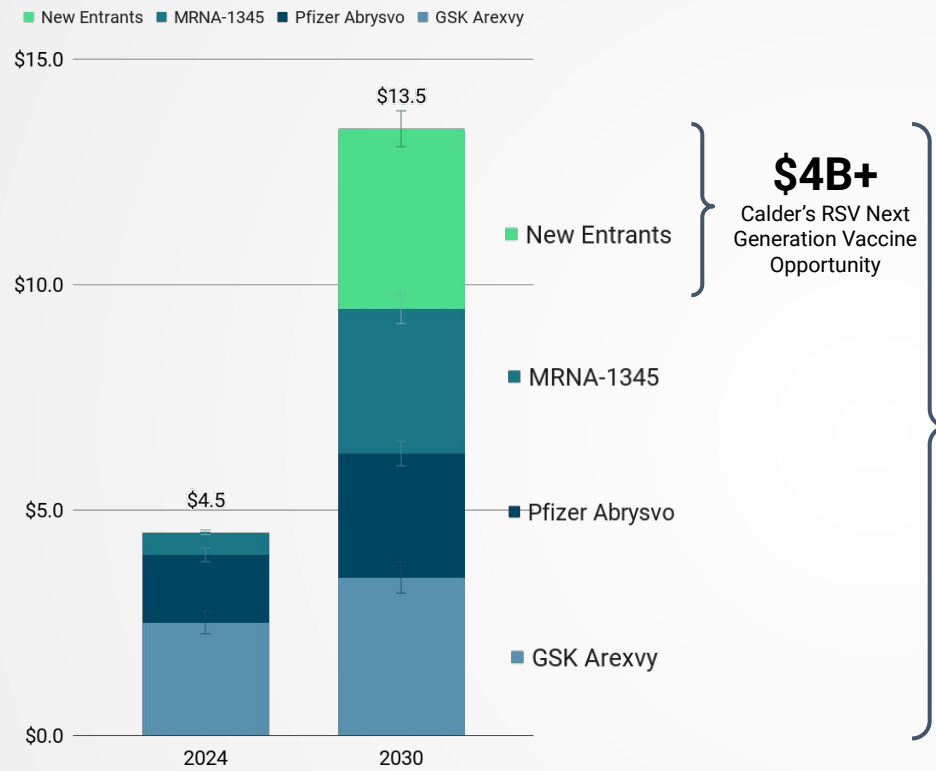
**Preclinical protection** CLD-001 fully protects against viral challenge.  
Cotton rats



**Remaining unmet needs** CLD-001's high potency improves protection of most vulnerable older adults.  
Addresses protection gaps in 1st generation.

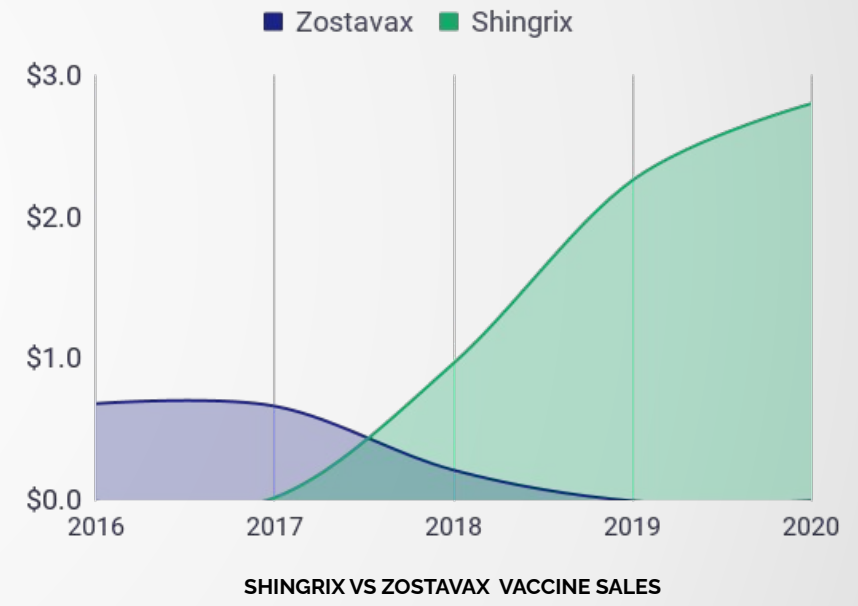
# MARKET OPPORTUNITY

Targeting older adults with greatest efficacy provides clearest path to overtaking lucrative markets



**\$13B+**  
Total RSV Market Vaccines

**Next generation vaccines with new technologies dominate sales and boost overall market potential**



**BREAKING**  
**GSK Boosts Profit Forecasts After 'Outstanding' RSV Vaccine Launch**

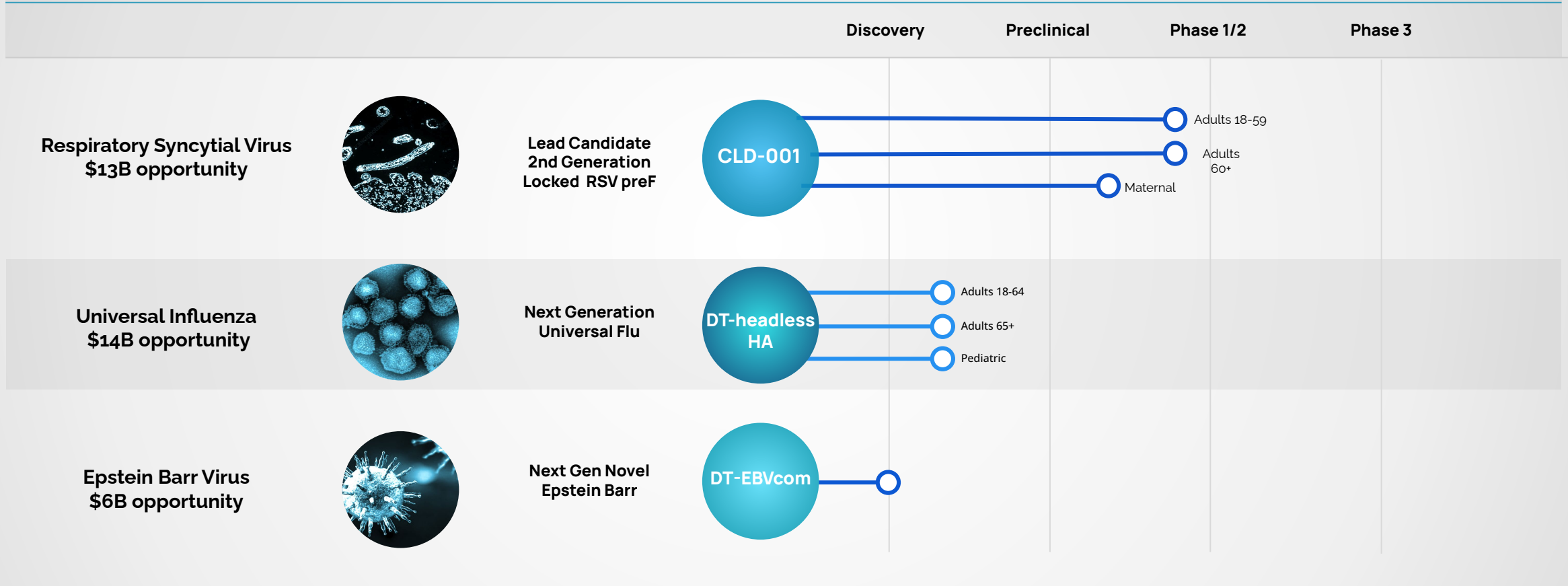
GSK Pulls Ahead of Pfizer in RSV Vaccine Market as Arexvy Nears Blockbuster Status  
Dec 01, 2023

**CDC/ACIP acts as sole buyer – next-gen vaccines with best safety & efficacy substantially outperform innovators – and expand the market**



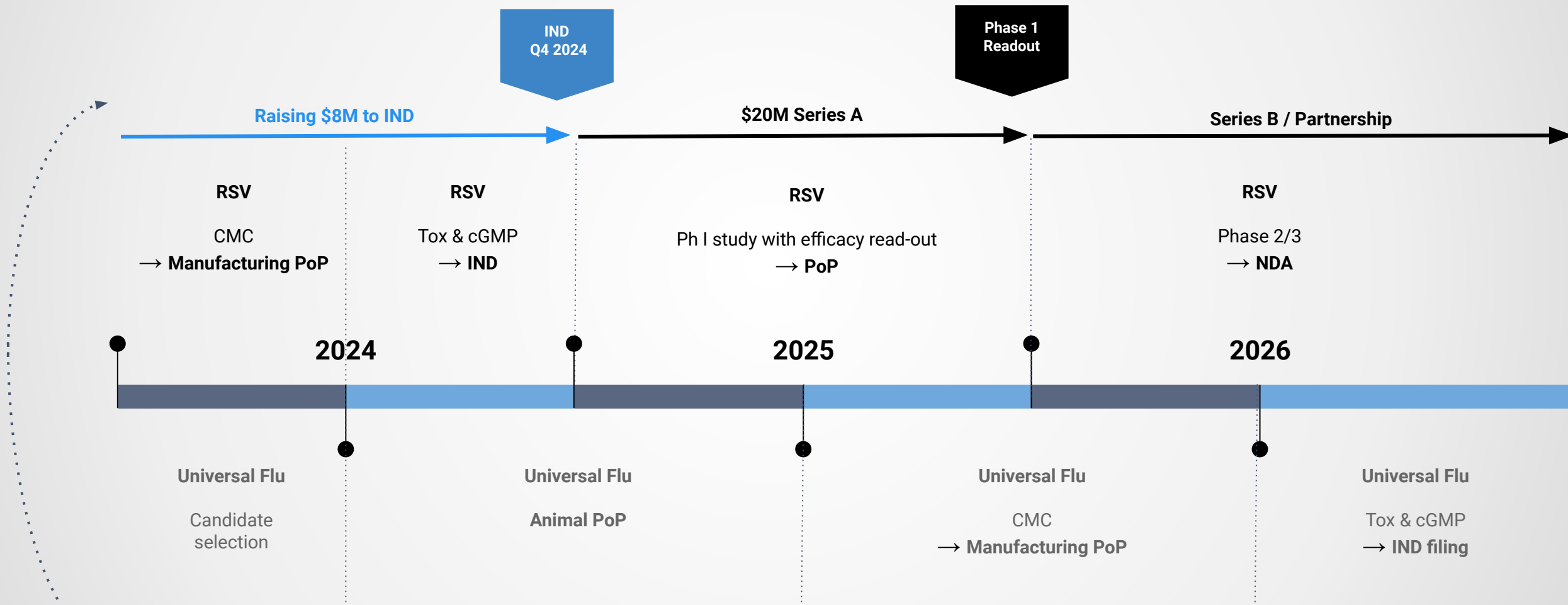
# PIPELINE

Universal flu vaccine and a preventative EBV vaccine would have



# TIMELINE

12 months to IND, 24 months to end of Phase 1b with PoP for Calder's RSV vaccine

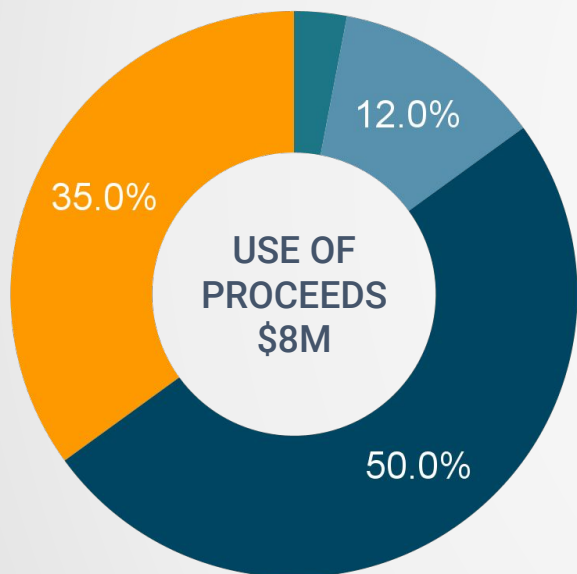


Of \$8M Seed round, \$6M+ (75%) indicated commitments. Seeking Lead investor.

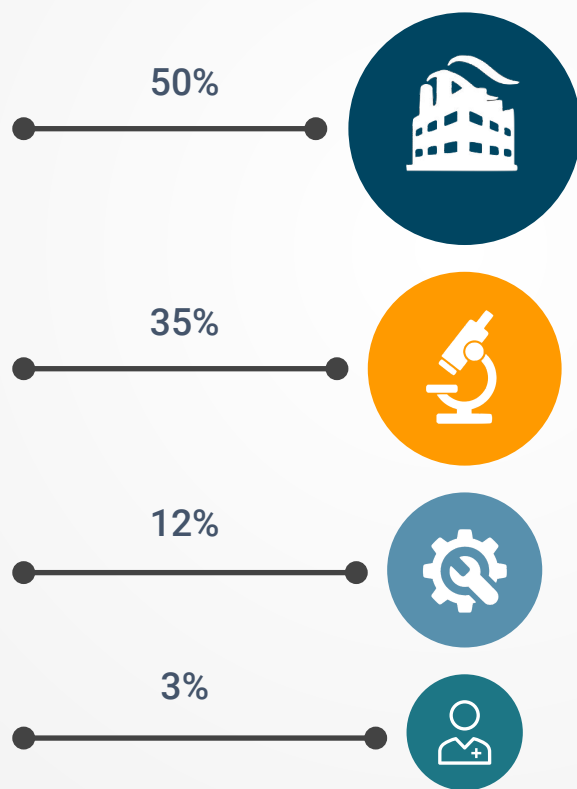
# USE OF PROCEEDS

Raising \$8M for R&D, cGMP, & Phase 1 Clinical PoP

Milestones achieve RSV manufacturing, IND & clinical proof of principle



- Regulatory 3%
- SG&A 12%
- CDMO 50%
- R&D 35%



## USE OF FUNDS

- CDMO: Biodextris MSA in place, tech transfer on-going; *milestones* – scaling, engineering run, cGMP manufacturing
- R&D: In-house & Outsourced R&D *milestone*: molecular PoP for U-flu program
- S,G&A: Overhead, rent, bus dev, corporate, legal, finance
- Regulatory Advisory: Technical and business KOL guidance, CMC & regulatory support

# TRACTION

Accomplishments, interest & commitments



**11.1x nAbs**

Best-in-class RSV results



**\$8.3M**

Non-Dilutive Grants



**\$8M to IND**

SOSV, NYS ESD,  
Genesis Consortium, etc



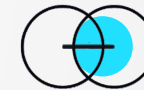
**3**

Accelerators



**7**

Issued US Patents



**Partnership Interest**

US, Canada, LatAm,  
China, India, S. Korea

## Recent Press

- Biodextris announces clinical supply agreement with Calder Biosciences [link](#)
- Check out IndieBio NY's latest cohort: [link](#)

# TEAM & ADVISORS

Deep expertise in protein chemistry, vaccine design, adjuvants, CMC, regulatory, clinical research, licensing & business development



Christopher Marshall, PhD  
Founder & CEO

THE ROCKEFELLER UNIVERSITY  
OLIVER WYMAN



Mark Yondola, PhD  
Co-founder & CSO

Mount Sinai



Dirk Pleimes, MD  
Chief Medical Officer

BAYER parexel  
myelo



Dan Catron, MBA  
Chief Operating Officer

Allele Biotechnology Scripps Research  
IQVIA CTMC+



Barry Buckland, PhD

MERCK



Florian Schödel, MD

MERCK



Jason S. McLellan, PhD

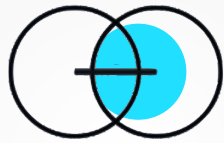
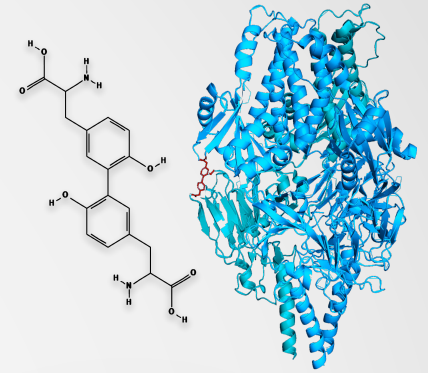
NIH 1997 TEXAS  
The University of Texas at Austin



Beth Junker, PhD

MERCK

# SUMMARY



## BEST-IN-CLASS VACCINE PLATFORM

Next generation fusion protein vaccines



## RSV IND BY END OF 2024

Lead RSV vaccine at clinical manufacturing stage



## RAISING \$8M TO IND

Clinical manufacturing, Tox, to IND



VRC/NIAD



SBIR-STTR



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NEW YORK STATE OF OPPORTUNITY  
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biodextris



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Crowe Lab



BETTER VACCINES,  
BETTER LIVES. ■



[www.CalderBiosciences.com](http://www.CalderBiosciences.com)



[linkedin.com/company/calder-biosciences-inc](https://www.linkedin.com/company/calder-biosciences-inc)



[crunchbase.com/organization/calder-biosciences-inc](https://www.crunchbase.com/organization/calder-biosciences-inc)

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+1-631-235-9397



VRC/NIH



SBIR · STTR



NIH  
NIAID



NEW YORK  
STATE OF  
OPPORTUNITY  
Empire State  
Development



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ENDLESS  
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biodextris



BioBAT

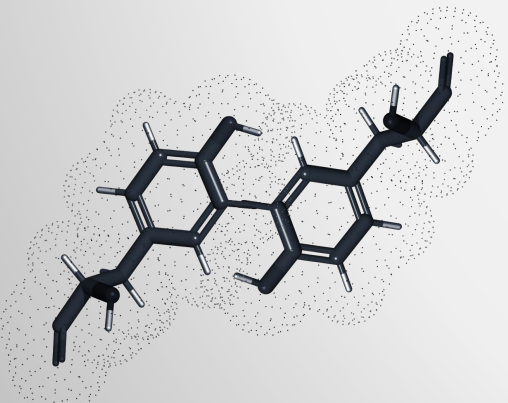
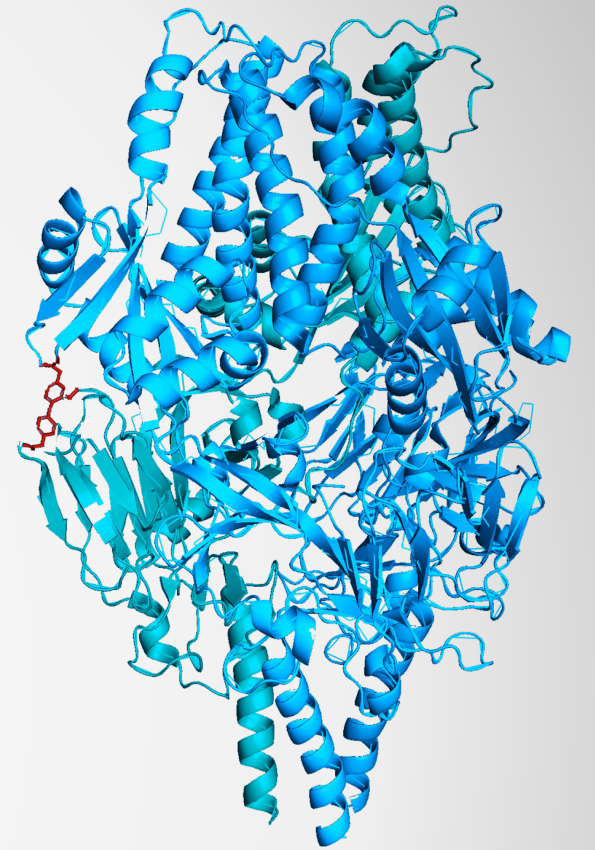


DOWNSTATE  
HEALTH SCIENCES UNIVERSITY



Crowe Lab

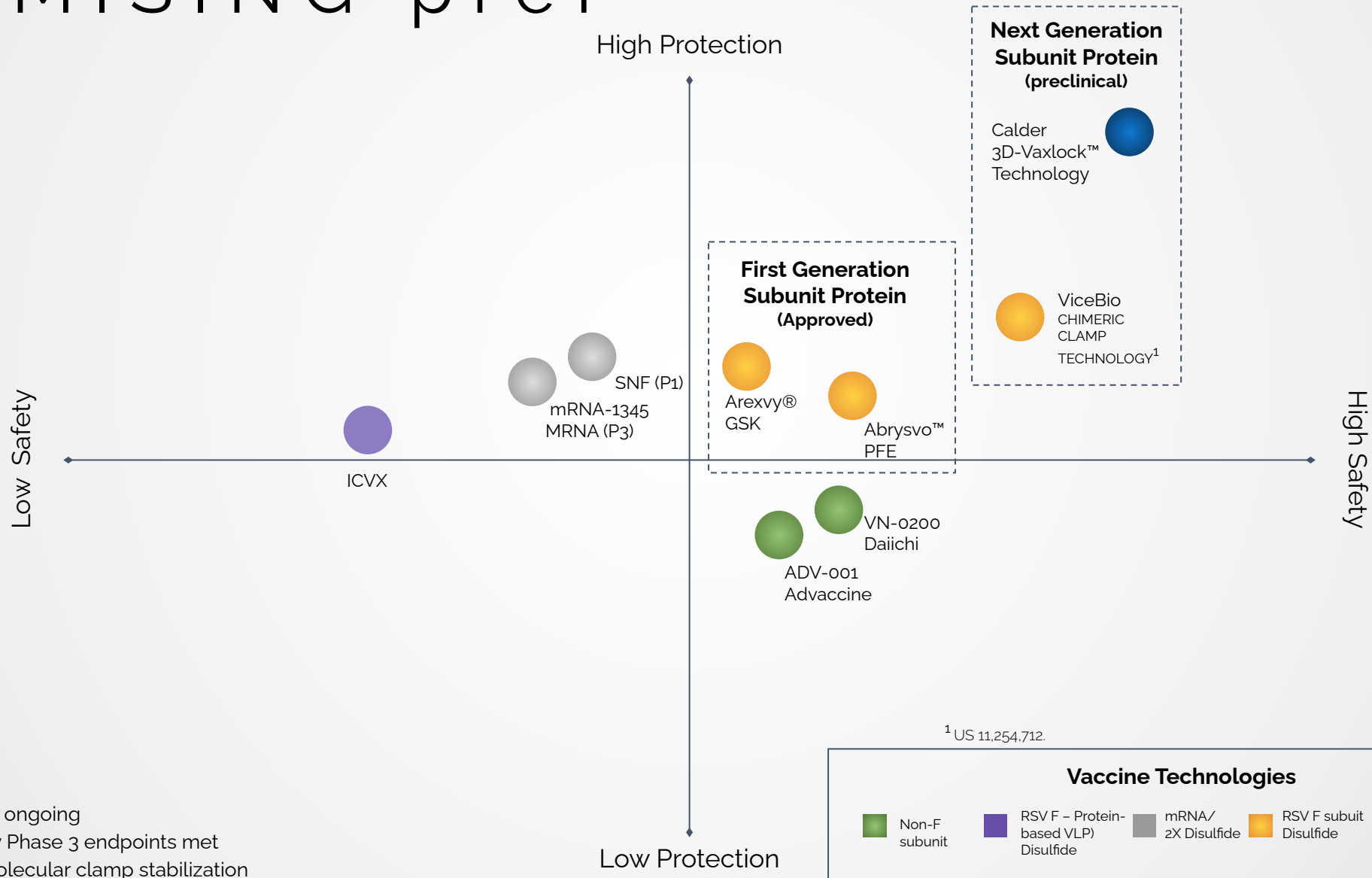
# APPENDIX. ■





# C D L-001 IS MOST PROMISING preF

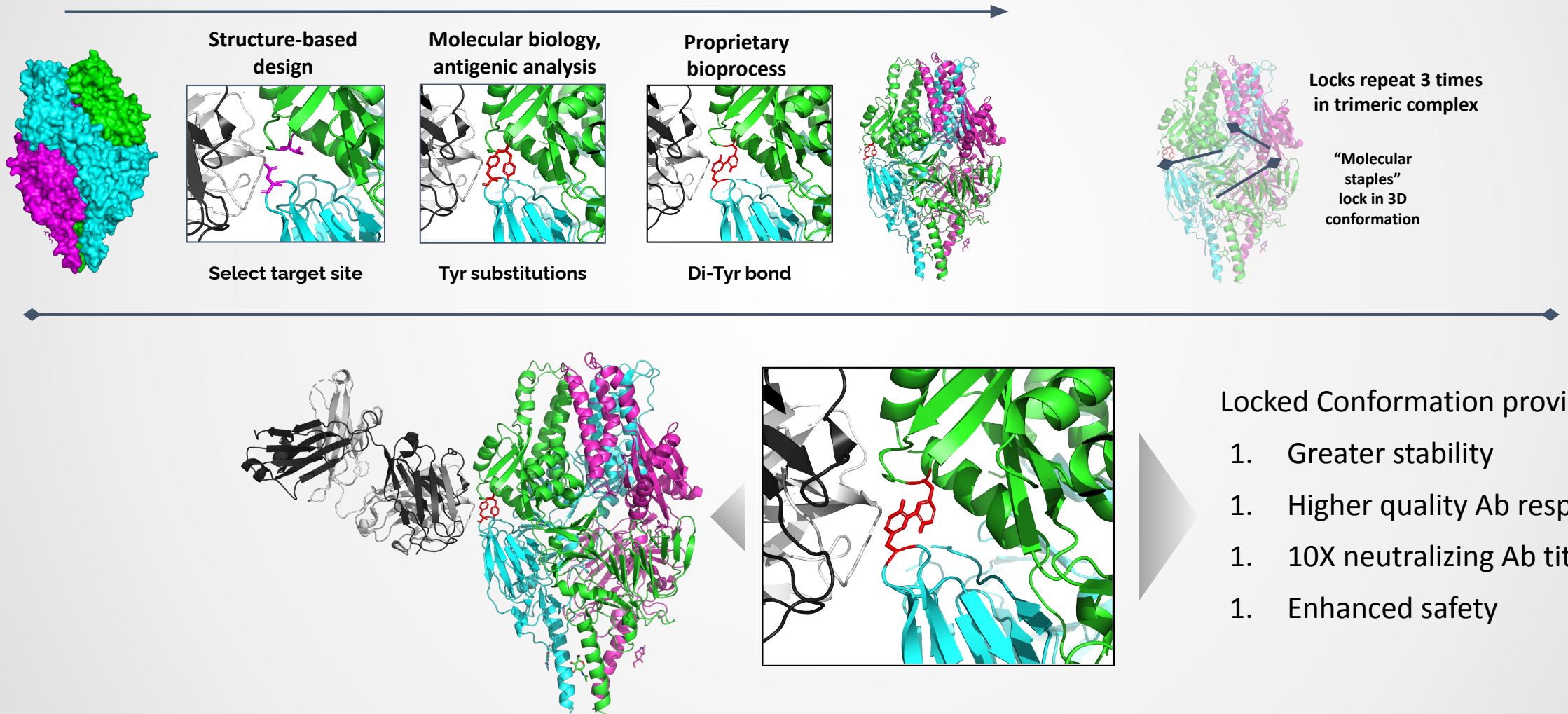
Preclinical results for Calder's preF vaccine promise good protection of most vulnerable older adults,



P1 = Phase 1 ongoing  
 P3 = primary Phase 3 endpoints met  
 Vicebio = molecular clamp stabilization

# TECHNOLOGY APPLICATION

3D-Vaxlock™ Technology locks vaccines in their most potent shape providing, highly immunogenic, safe and protective viral protein-based vaccines



# MARKETS

Huge opportunities in novel viral surface protein vaccines. Trending upward due to increased recognition, higher pricing and substantial reimbursement.

## TOTAL ADDRESSABLE MARKET

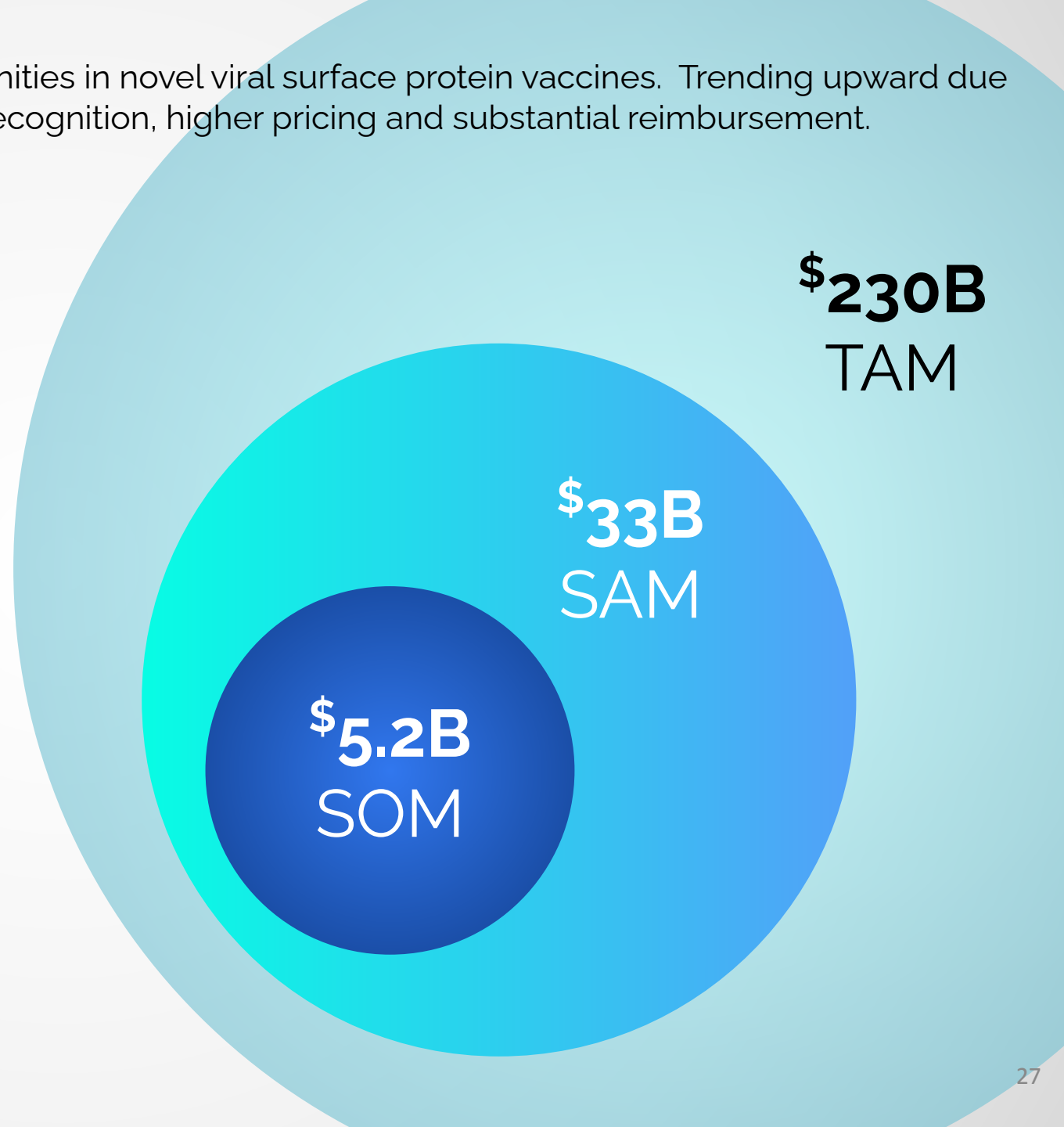
TAM: Global vaccine sales by 2030

## SERVICEABLE ADDRESSABLE MARKET

SAM: Global vaccine sales \$13B RSV, \$14B Influenza, \$6B EBV

## SERVICEABLE OBTAINABLE MARKET

SOM: Market share of 22.5% RSV, 10% influenza, & 15% EBV vaccine sales



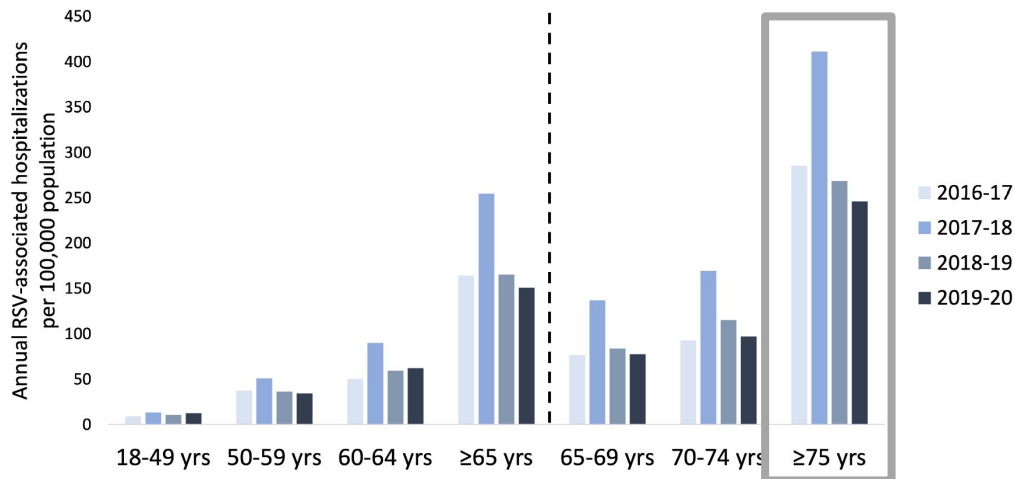
# RSV UNMET NEEDS

CDC Evidence to Recommendations Framework highlights insufficient data & durability issues

## Unmet needs: Efficacy & Durability in the 75+ age group

**CDC Published & Unpublished Data: GSK 33.8% Efficacy 80+ and 49.3% Efficacy 75+ Pfizer neutralizing antibody titers decline 75-80% over 12m**

**RSV-NET estimated annual hospitalizations per 100,000 adults: 2016–2017 to 2019–2020**



25

CDC RSV-NET unpublished data. Estimates are adjusted for under-testing and incomplete test sensitivity. <https://www.cdc.gov/rsv/research/rsv-net/index.html>

### GSK: RSV lower respiratory tract disease (LRTD)

Age group in years	Case split (vaccine/placebo) <sup>a</sup>	Manufacturer-calculated vaccine efficacy <sup>b</sup> , % (CI)	
		No adjustment by season	Adjusted by season
≥60 (all)	30/139	74.5 (60.0, 84.5)	67.2 (48.2, 80.0)
≥65	25/100	70.3 (53.5, 81.6)	61.2 (39.0, 76.1)
≥70	13/65	76.4 (56.7, 88.1)	69.3 (43.4, 84.6)
≥75	8/24	Not shared <sup>c</sup>	49.3 (-18.2, 80.6) <sup>c</sup>
≥80	4/10	52.6 (-64.2, 89.2) <sup>c</sup>	38.4 (-118, 86.1) <sup>c</sup>

<sup>a</sup> GSK pivotal phase 3 trial (Papi A, et al. NEJM 2023 <https://doi.org/10.1056/nejmoa2209604>). Events of each outcome were included if they occurred on or after day 15 after injection. Median time, across participants, of efficacy follow up was 17.8 months, including unpublished data provided by manufacturer from season 2. Total 24,967 participants (31,932 person-years) under surveillance.

<sup>b</sup> Calculated using Poisson model, adjusted by season and participant age and region. Adjustment by season resulted in efficacy estimates substantially different from those estimated by CDC. Due to exclusion of follow up time after dose 2 of RSVPreF3 among participants randomized to annual re-vaccination, person-time follow up in the placebo arm exceeded that in the intervention arm.

<sup>c</sup> Highlighted text indicates that evidence of statistically significant efficacy is lacking.

37

# CLD - 101 STABILITY

Calder 4x Arexvy, 5x Abrysvo & 11.1x DS-Cav1 nAbs;  
highest melting pt – 79.53°C

## Immunogens with greatest stability and structural fidelity elicit highest nAb titers

Company	RSV Vax Sales Annual (Est)	Vaccine	Status	Private Sector Cost/Dose	nAbs (Fold over DS-Cav1)	DSF Melting Pt.	Technology	Precursor
Calder		CLD-001	Active	-	11.1	79.53°C	Recombinant Protein (Dityrosine)	Cav1
GSK	\$3.7B	Arexvy®	Launched-2023	\$280.00	2.7	Not disclosed	Recombinant Protein (Disulfide)	DS-Cav1
PFE	\$2.5B	Abrysvo™	Launched-2023	\$295.00	2.2	69.20°C	Recombinant Protein (Disulfide)	DS-Cav1
MRNA	\$3.1B	mRNA-1345	Active-2024	-	(1.0)	52.90°C	mRNA	DS-Cav1
NIH		DS-Cav1	Licensed	-	1.0	52.90°C	Recombinant Protein (Disulfide)	RSV F

# CALDER ADVANTAGE

Highest stability drives best safety and efficacy

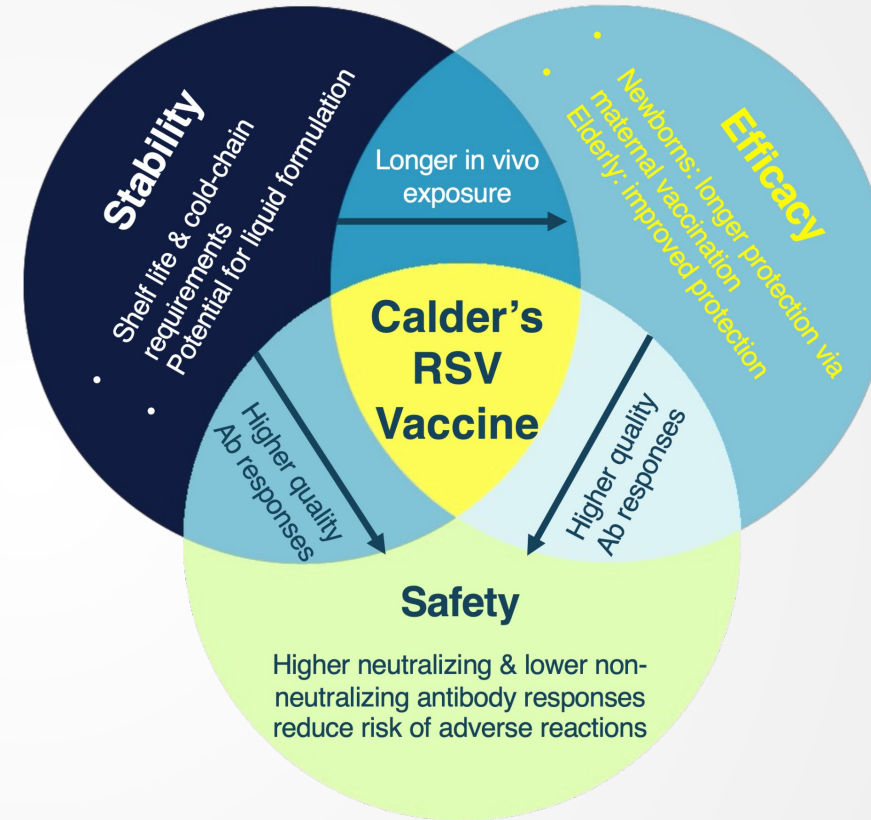


## Calder's RSV Vaccine Origins:

Calder's 3D-Vaxlock™ was applied in HIV vaccine research (BMGF+IAVI funding/collaboration)

Calder initially collaborated with Jason McLellan (VRC) to stabilize HIV Env

Then Calder, Barney Graham (VRC) and Jason McLellan (Dartmouth, then UT Austin, Calder SAB member) entered a long-term 3-way collaboration to apply Calder's 3D-Vaxlock™ and increase stability, safety & efficacy of RSV preF vaccine immunogen.



50+ Years in the Making, RSV Vaccine Arrives | August 09, 2023

Forest W. Arnold, DO, MSc; Barney S. Graham, MD, PhD

<https://www.medscape.com/viewarticle/985981>

RSV vaccines: the latest success story | Jason McLellan explains the breakthroughs that paved the way | March 14 2023

<https://www.iavi.org/iavi-report/rsv-vaccines-the-latest-success-story>

# PROTEIN VS. mRNA

Both geared to focus responses. Protein vaccines more potent & tolerable – preferable where speed & adaptability less important

## Short Development Timelines

Very short timelines - rapid pandemic responses

### Good Efficacy

Lower dose, self-adjuvanting. Reasonable Ab and CD8+ T cell responses.

### Low Tolerance

High frequency of systemic cold-like responses and moderately severe injection site reactions

### Low Stability

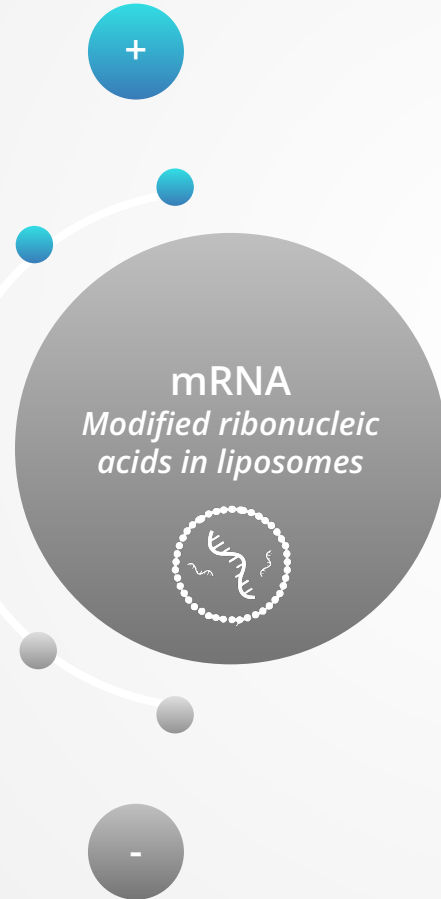
short shelf-lives & difficulties in distribution (-80°C storage)

### Low Durability

Short period of protection

### Limited Regulatory Experience

Covid-19 Vaccine (BioNTech & Moderna)  
RSV Vaccine (Moderna)



VS

## Moderate Development Timelines

New technology enables shorter timelines

### High Efficacy

High-dose → most potent Ab responses. Potent CD8+ T cell responses with good adjuvants

### High Tolerance

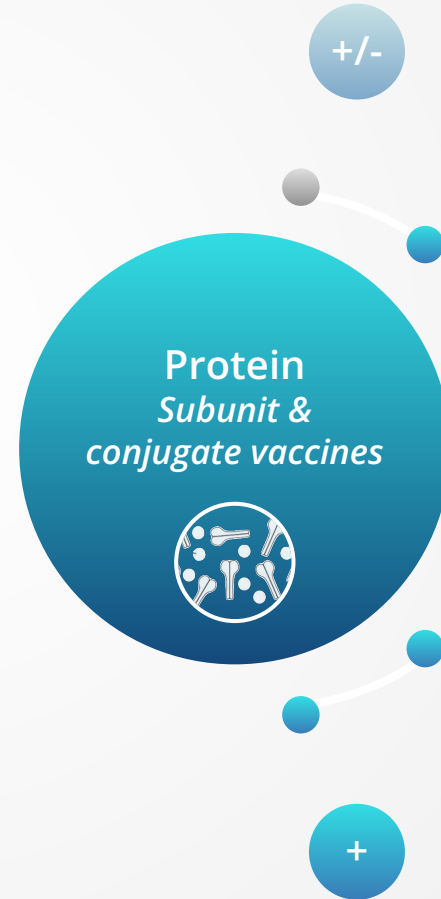
Dependent on selection of adjuvant

### Good Stability

Good shelf-lives & ease of distribution (see below)

### High Durability

Longevity of protection



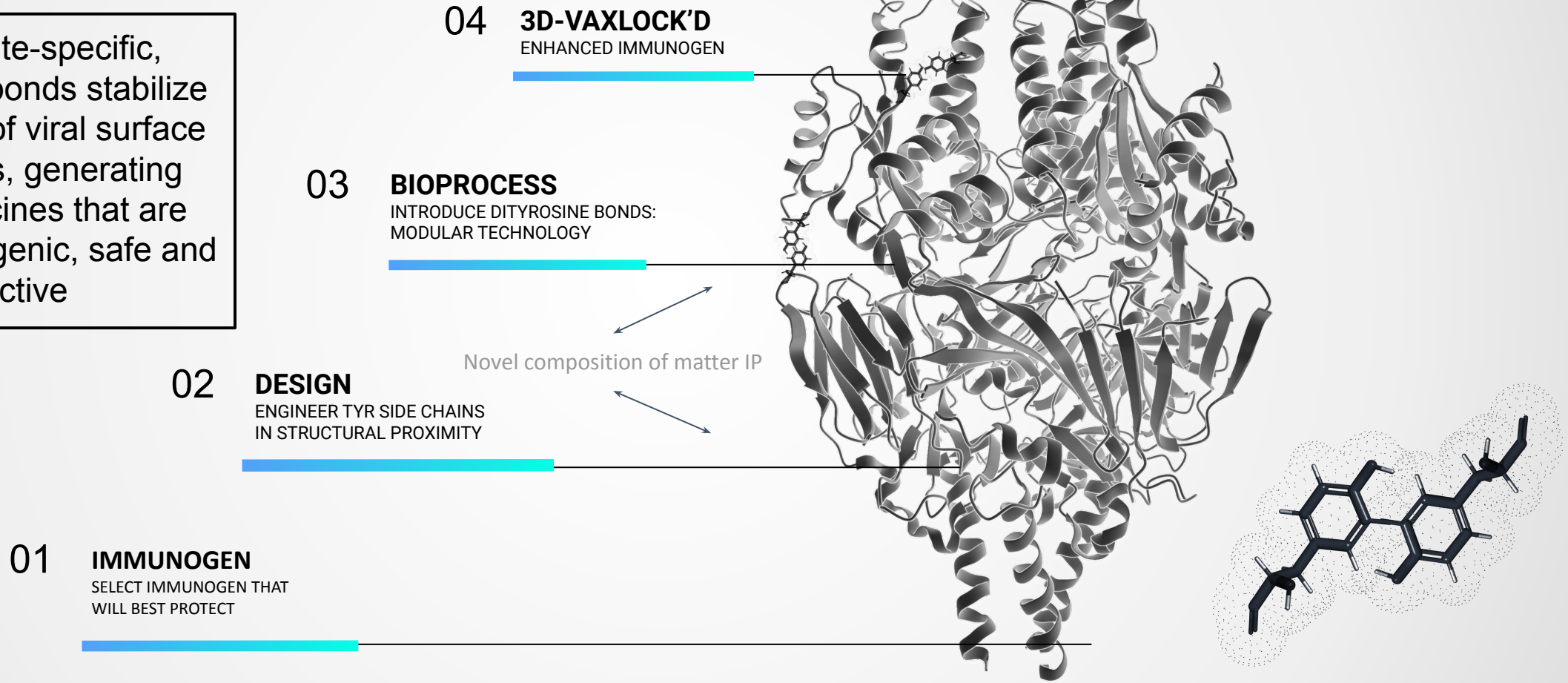
### Extensive Regulatory Experience

~50% of childhood vaccines  
HIB vaccine, Recombivax-HB, Prevnar, Gardasil, meningitis vaccines, whooping cough vaccine, Flublok, Shingrix, RSV vaccines (Pfizer & GSK)

# CALDER'S BEST-IN-CLASS VACCINE TECHNOLOGY

Proprietary 3D-Vaxlock™ Platform Technology *locks* vaccines in their most potent shape

Targeted, site-specific, covalent C-C bonds stabilize conformation of viral surface glycoproteins, generating superior vaccines that are highly immunogenic, safe and protective



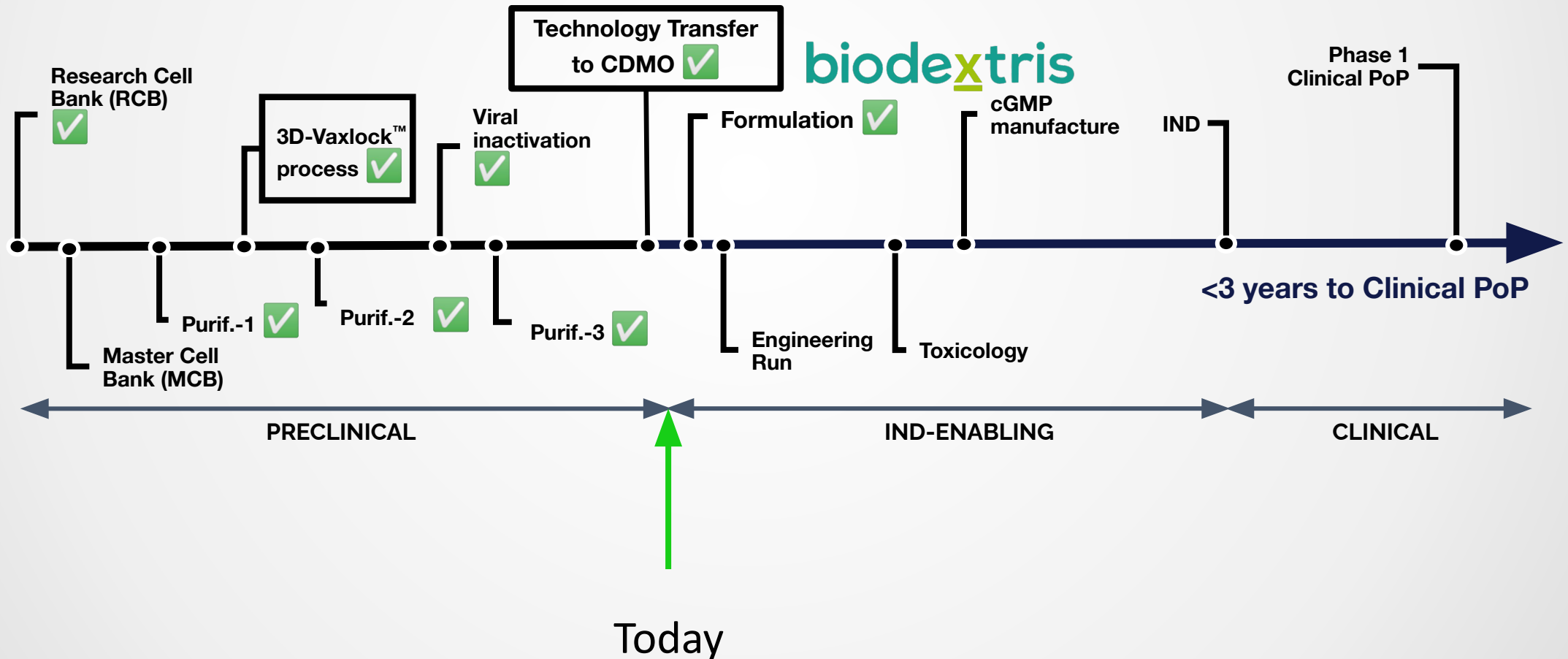
TARGETED CROSS-LINKING CAN BE APPLIED BROADLY IN PROTEIN ENGINEERING



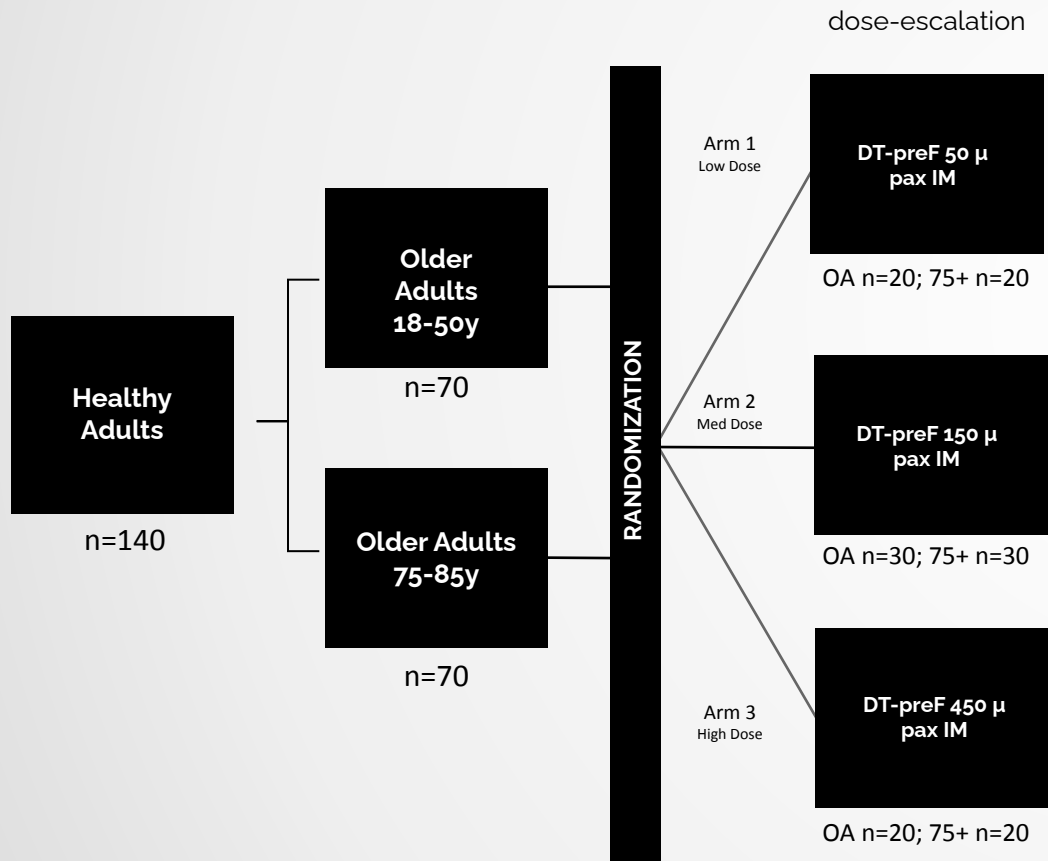
# CDMO & CRO

RSV vaccine manufacturing and development in place

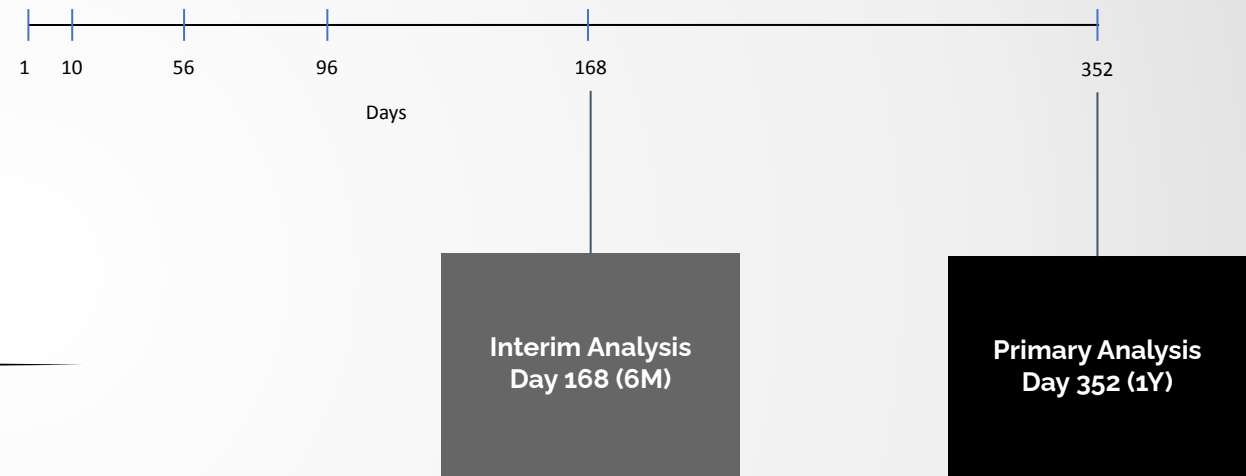
**Calder's processes & analytics have been transferred to clinical manufacturing**



# PHASE 1b SCHEMATIC



Demonstrate Best-in-class and "First-in-class" in target populations in Phase 1b

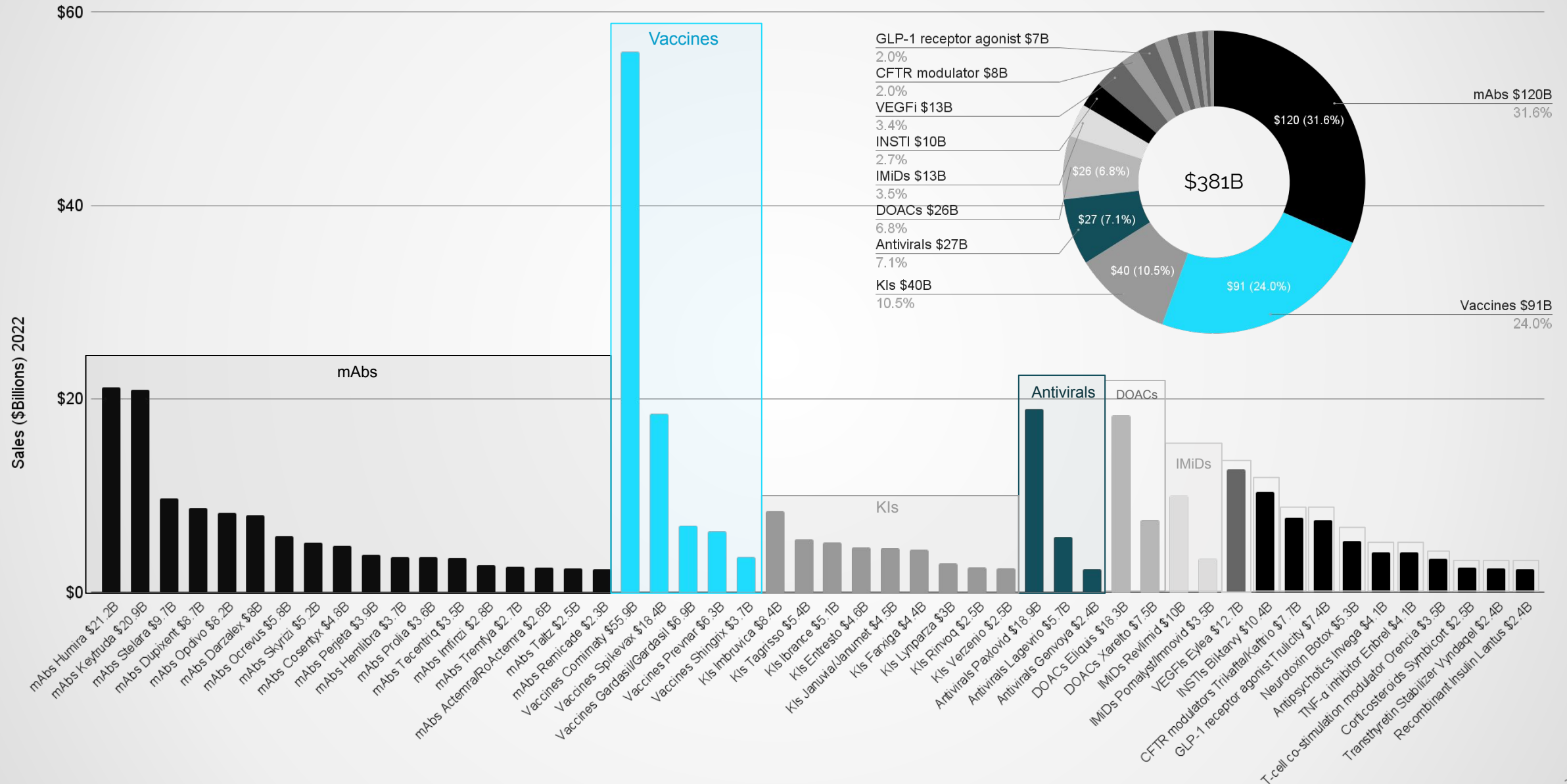


1 Year-Phase 1b clinical trial establishes safety and immunological PoP with **neutralizing Ab titers**.

Unmet needs met in target older adult populations

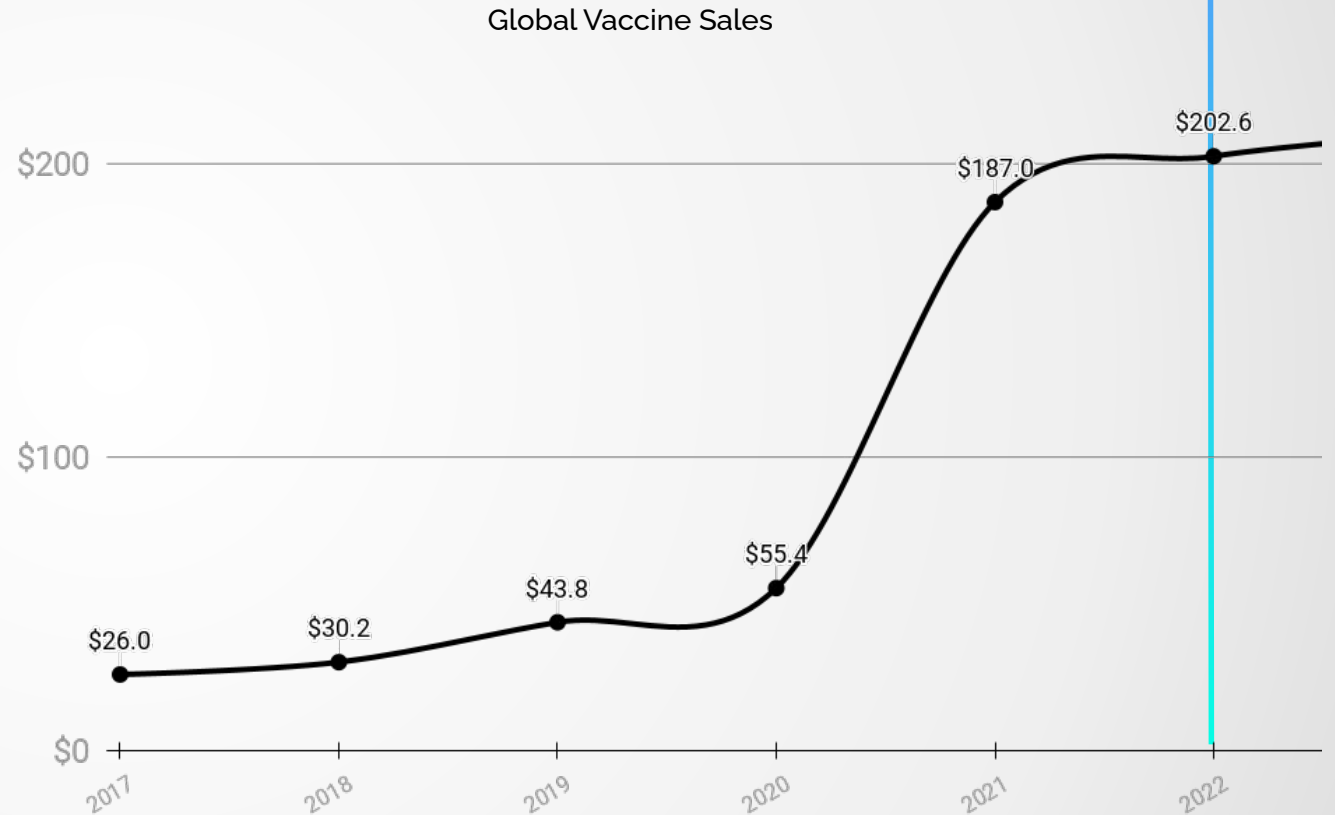
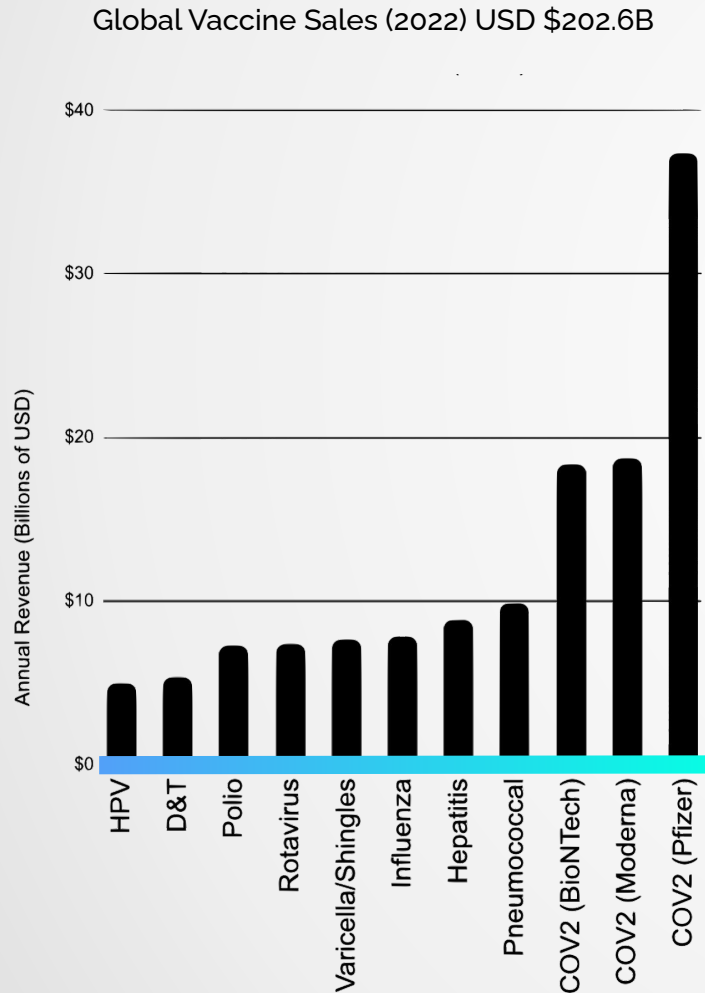
# STRONG SALES

Vaccines #2 category of top 50 best selling pharmaceuticals. 5 brands = \$91B revenue (2022)



# BLOCKBUSTER POTENTIAL

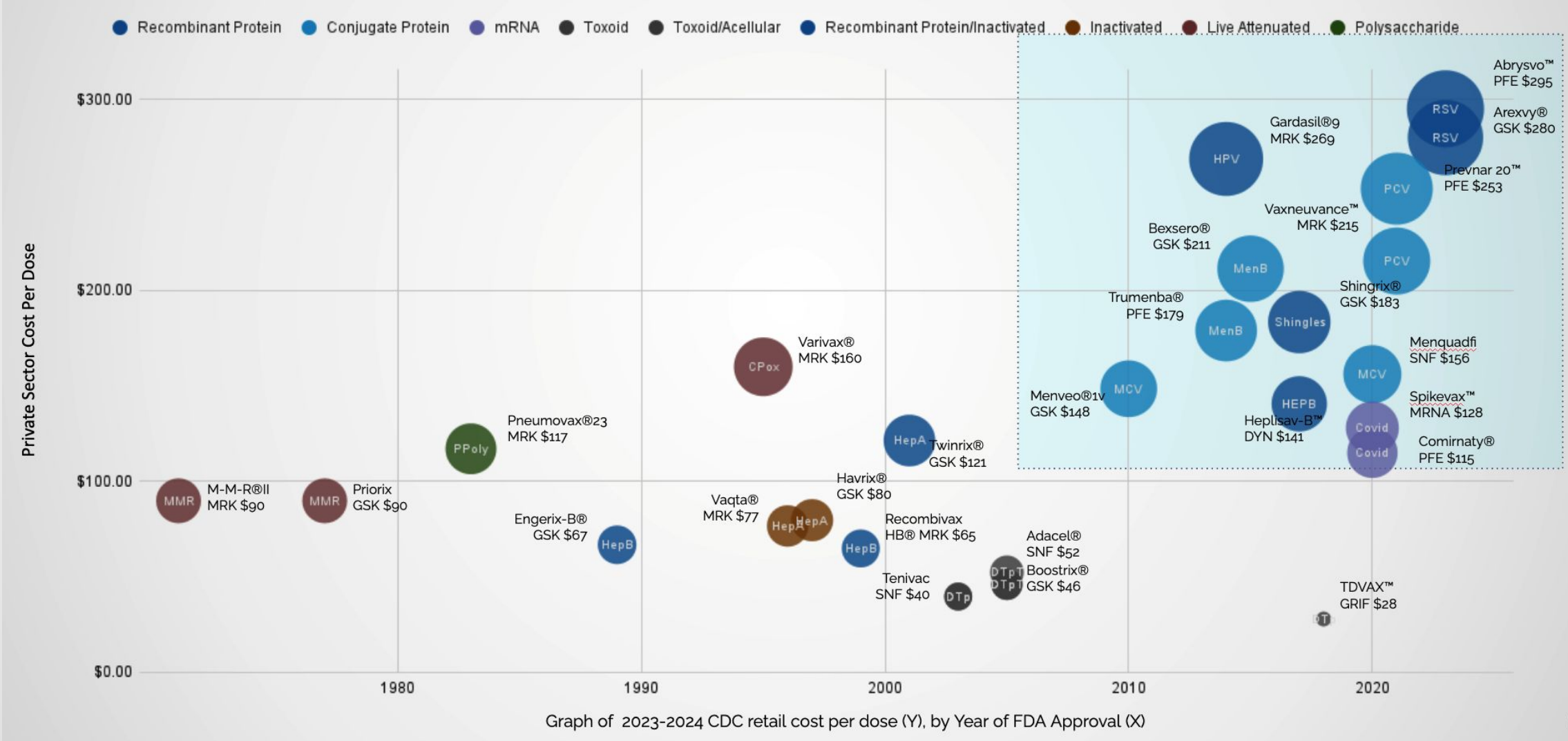
Covid reminded us that vaccines remain one of the most important means of protecting and improving lives



*Post-pandemic blockbuster demand for vaccines emergence*

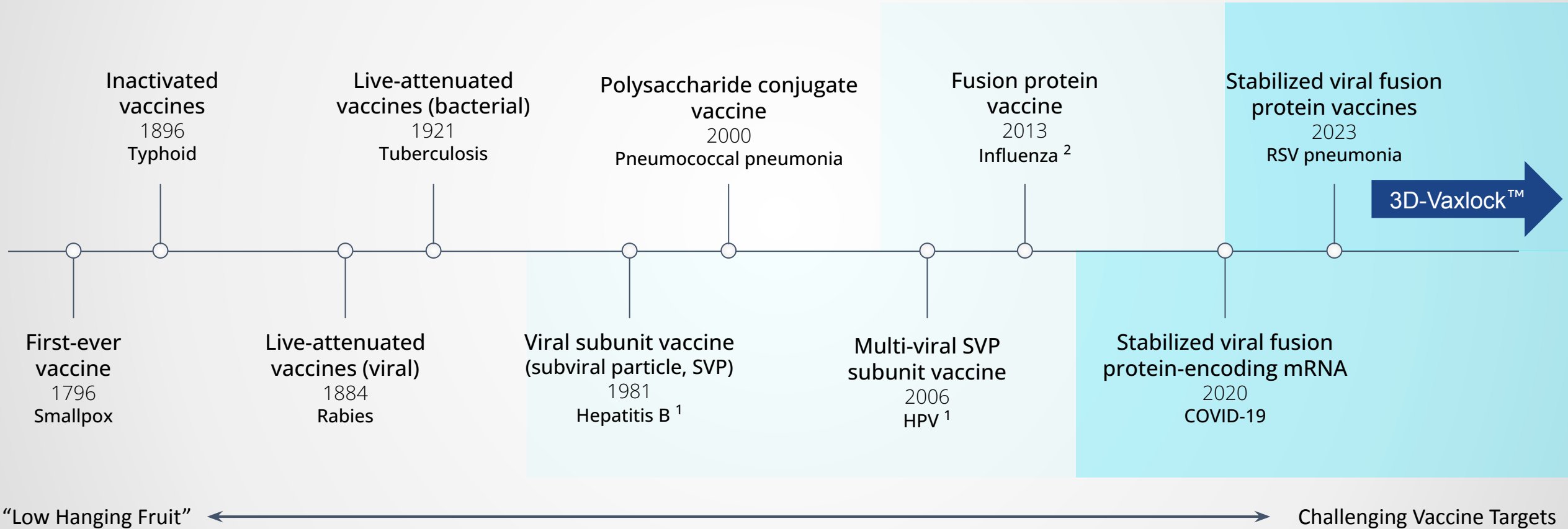
# ACCELERATING OPPORTUNITY

Vaccine reimbursement/pricing rising since before the pandemic. *Unaffected by IRA legislation.*



# VACCINE EVOLUTION

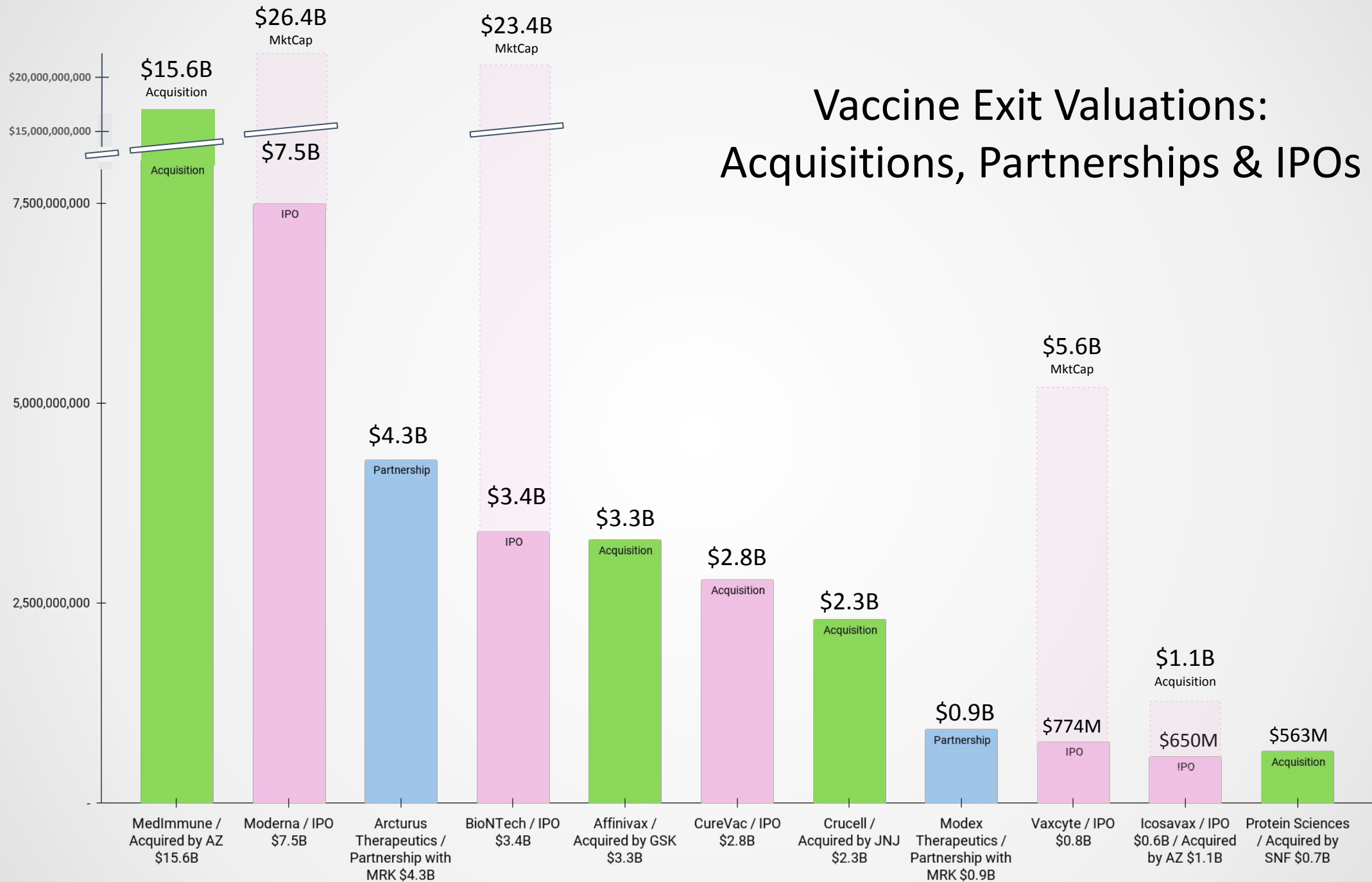
Increasingly challenging vaccine targets require increasingly sophisticated and powerful vaccine technologies



<sup>1</sup> conformationally stabilized by subvirus particle technology

<sup>2</sup> conformationally stable fusion protein, stabilization not required

# Vaccine Exit Valuations: Acquisitions, Partnerships & IPOs



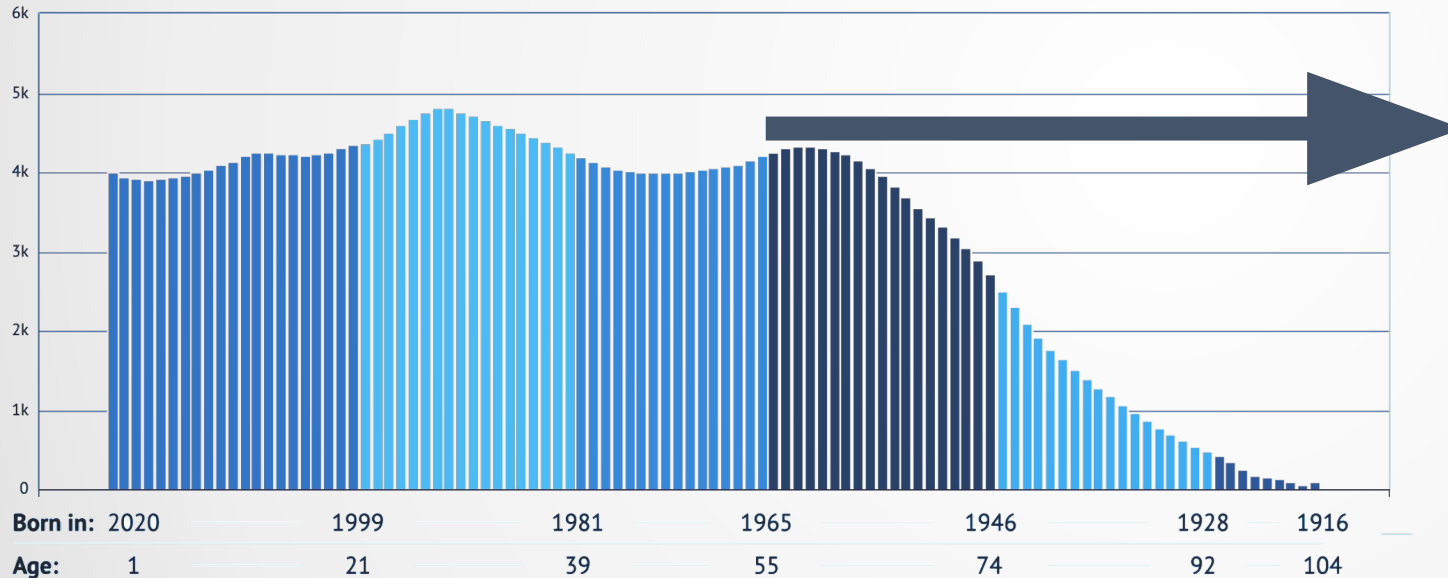
# WHY NOW?

Aging population born well before current vaccines approved. Legislation mandating vaccine requirements & enforcement already happening

“The most formidable demographic challenge facing the world today is no longer rapid population growth, but population aging.”

David E Bloom & Leo M Zucker, *IME*, June 2023

Total US Population by Age in 2020  
*thousands*

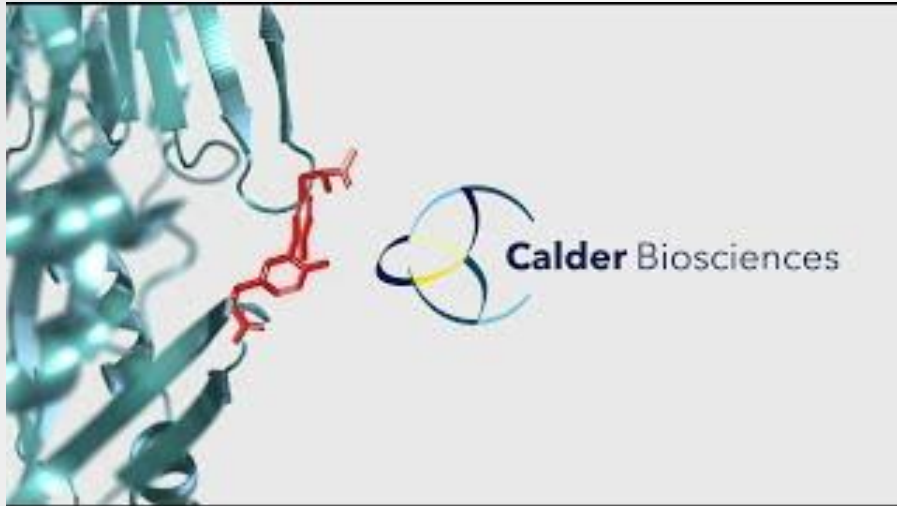


GEN-Z	MILLENNIALS	GEN-X	BABY BOOMERS	SILENT GEN	GREATEST GEN
86.40M	82.22M	65.13M	68.70M	23.63M	1.75M
Born 2000-2020	Born 1982-1999	Born 1966-1981	Born 1947-1965	Born 1929-1946	1916-1928

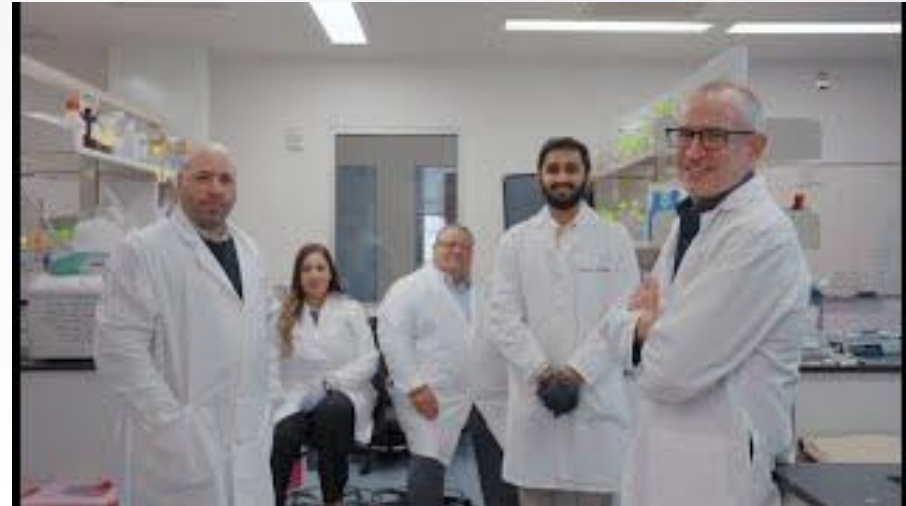
Target	Tradename	Year Approved
Respiratory Syncytial Virus bivalent	Abrysvo	2023
Respiratory Syncytial Virus A	Arexvy	2023
Zoster Vaccine Recombinant, Adjuvanted	Shingrix®	2017
HPV-Human Papillomavirus 9-valent	Gardasil®9	2014
Pneumococcal 20-valent	Prevnar 20™	2021
Pneumococcal 15-valent	Vaxneuvance™	2021
Pneumococcal Polysaccharide 23-valent	Pneumovax®23	1983
MENB – Meningococcal Group B	Bexsero®	2015
MENB – Meningococcal Group B	Trumenba®	2014
Meningococcal Conjugate (A, C, W,Y)	Menquadfi	2020
Meningococcal Conjugate (A, C, Y, W-135)	Menveo® 1vial	2010
Covid-19	Spikevax™	2020
Covid-19	Comirnaty®	2020
Hepatitis B Adult	Hepelisav-B™	2017
Hepatitis A-Hepatitis B Adult	Twinrix®	2001
Hepatitis A Adult	Havrix®	1995
Hepatitis A Adult	Vaqta®	1996
Hepatitis B Adult	Engerix-B®	1989
Hepatitis B-Adult	Recombivax HB®	1999
Tetanus, Diphtheria, Pertussis	Adacel®	2005
Tetanus, Diphtheria, Pertussis	Boostrix®	2005
Tetanus, Diphtheria, Pertussis	Boostrix®	2005
Tetanus and Diphtheria Toxoids	Tenivac	2003
Tetanus and Diphtheria Toxoids	Tenivac	2003
Tetanus and Diphtheria Toxoids	TDVAX™	2018
Varicella	Varivax®	1995
Measles, Mumps and Rubella (MMR)	Priorix	2022
Measles, Mumps, & Rubella	M-M-R®II	1971



# DEMO VIDEOS



Calder 3D-Vaxlock™ Technology Explainer



Calder Science Team & Technology



Intro to Calder Biosciences vaccines



SOSV IndieBio Demo Day 2023