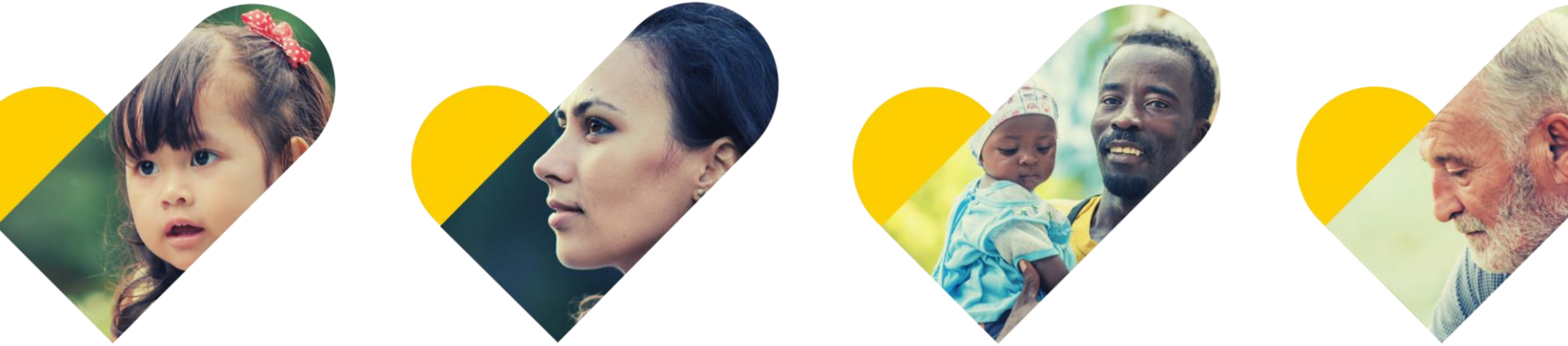

# Pioneering the science of breaking immune tolerance

## JPM Healthcare Conference 2024

January 11, 2024

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# Forward Looking Statements and Disclaimer

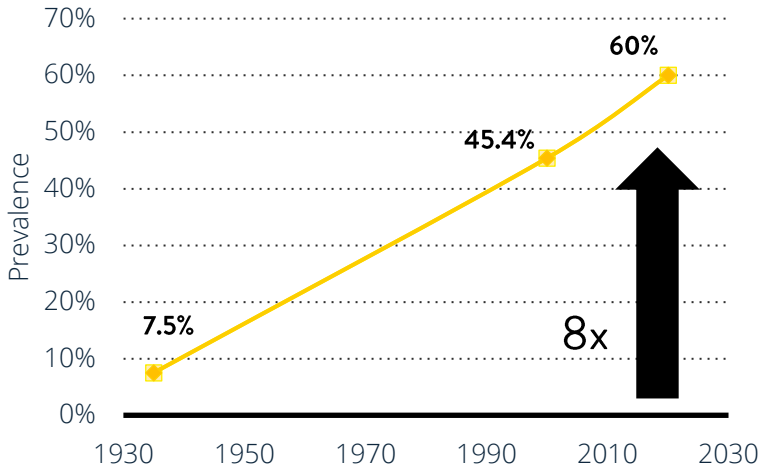
This presentation contains forward-looking statements within the meaning of the federal securities laws. Forward-looking statements generally are accompanied by words such as “will,” “could,” “aim,” "expect," “continue,” “plan,” "target," “potential,” "milestone," "opportunities," and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include statements regarding our discovery, research and development activities, in particular our development plans for our product candidates and potential future candidates, including anticipated clinical development timelines, and the potential for such product candidates to be used to treat human disease. These statements are based on various assumptions, whether or not identified in this presentation, and on the current expectations of management. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as, and must not be relied on as, a guarantee, an assurance, a prediction, or a definitive statement of fact or probability.

Actual events and circumstances are difficult or impossible to predict and will differ from assumptions. These forward-looking statements are subject to a number of risks and uncertainties discussed in our Annual Report on Form 10-K for the year ended December 31, 2022 and Form 10-Q for the quarter ended September 30, 2023, which have been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov. Actual results could differ materially from the results implied by these forward-looking statements. There may be additional risks that we presently do not know, or that we currently believe are immaterial, that could also cause actual results to differ from those contained in the forward-looking statements. In addition, forward-looking statements reflect our views and expectations, plans, or forecasts as of the date of this presentation. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so, except as required by law. These forward-looking statements should not be relied upon as representing our assessments of any date subsequent to the date of this presentation.

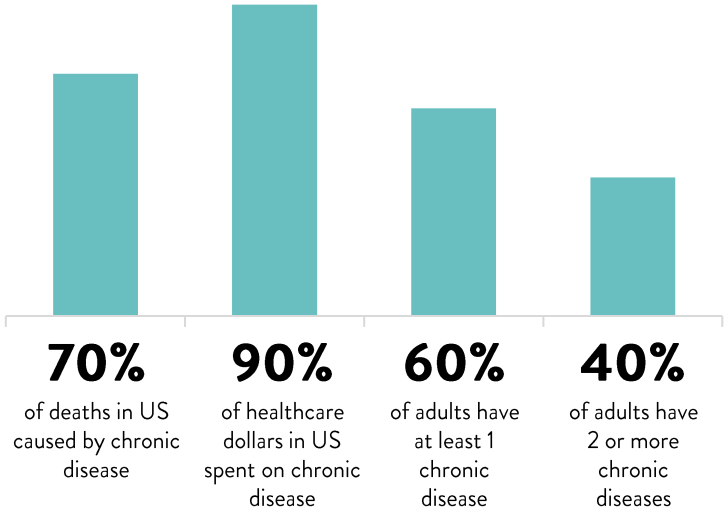
# Why what we do matters

# More people are suffering from chronic diseases than ever before

## Rising Chronic Disease Prevalence in US




## Today's chronic disease epidemic

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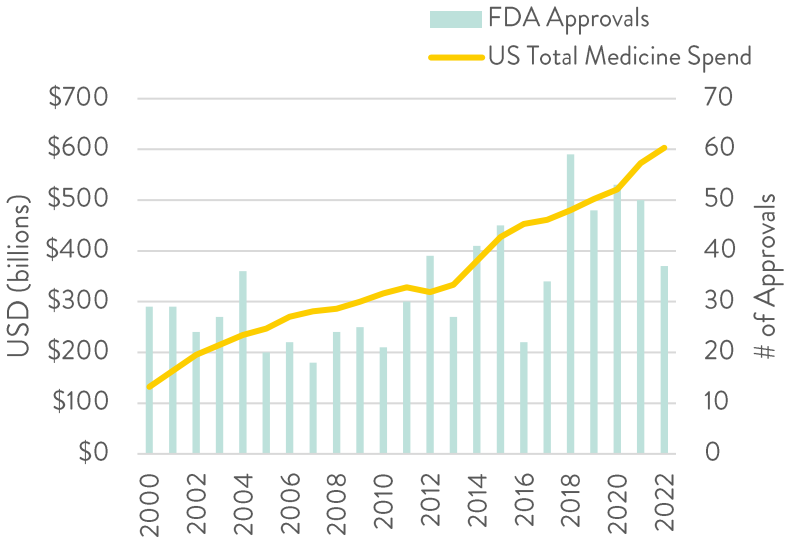
Sources: CDC, Weisz (2011)

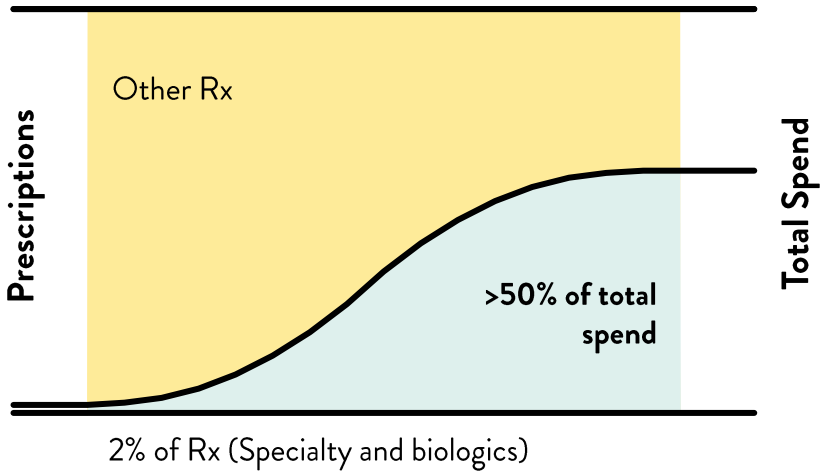
# Since 2000, more than 700 new drugs have been approved by FDA and drug spending has soared over 3X to $600B

## Drug spending has soared with new approvals




**$222k** Median price of new drug (2023)

## Majority of spend driven by specialty and biologics

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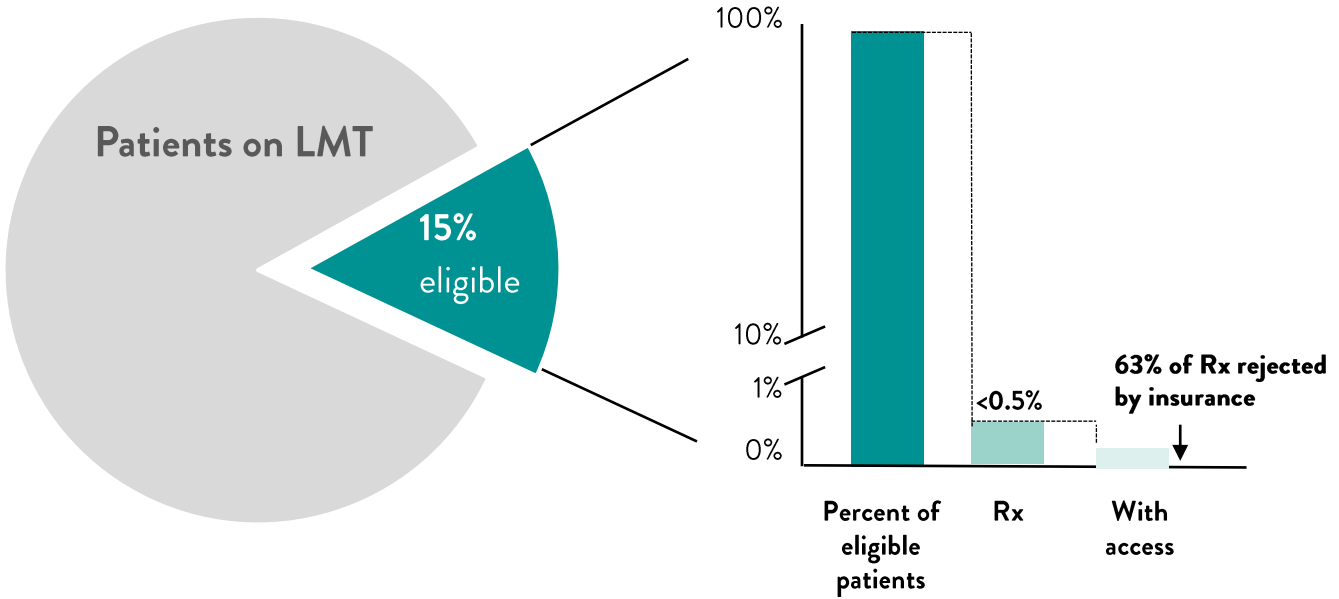
Source: IQVIA

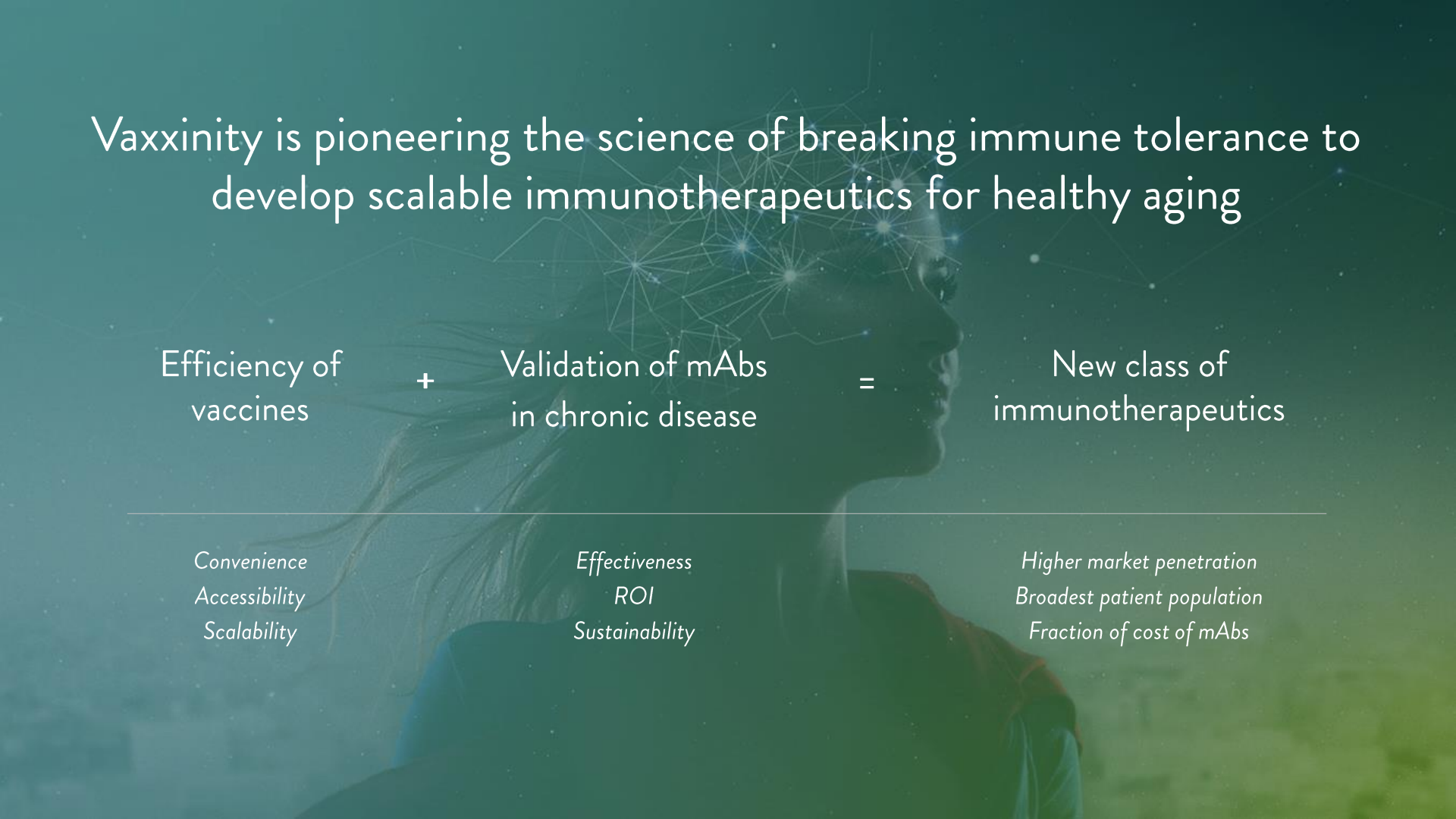
# Medicine is only as effective as its access

Effectiveness =
Efficacy x Access

**Example: PCSK9 Inhibitor Antibodies**




Source: Keralis et al. (2018)



# Vaxxinity is pioneering the science of breaking immune tolerance to develop scalable immunotherapeutics for healthy aging

| Efficiency of vaccines | + | Validation of mAbs in chronic disease | = | New class of immunotherapeutics |
|---|---|---|---|---|
| *Convenience*<br>*Accessibility*<br>*Scalability* | | *Effectiveness*<br>*ROI*<br>*Sustainability* | | *Higher market penetration*<br>*Broadest patient population*<br>*Fraction of cost of mAbs* |

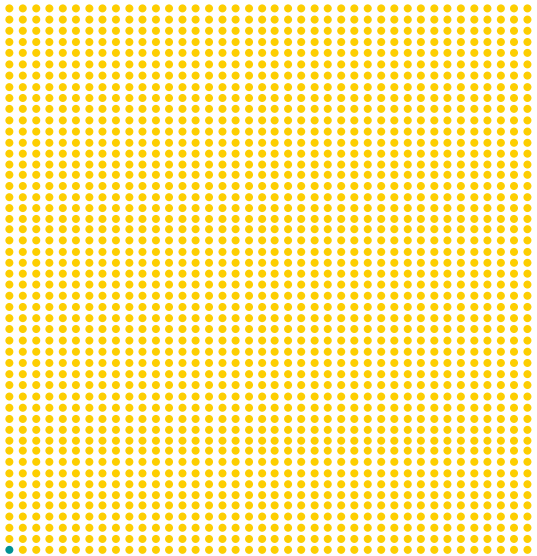
# Core advantages over traditional antibody immunotherapeutics

**>100X**

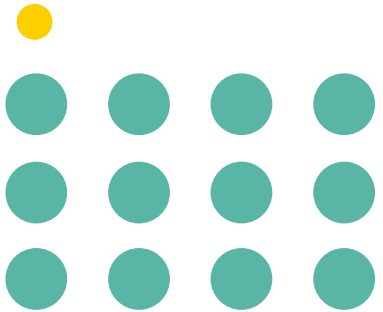
**MORE COST-EFFECTIVE**

**>1000X**

**MORE SCALABLE**



**MORE CONVENIENT and ACCESSIBLE**



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# Vaxxinity can expand the efficiency of vaccines beyond anti-infectives

- Aberrant or misfolded proteins

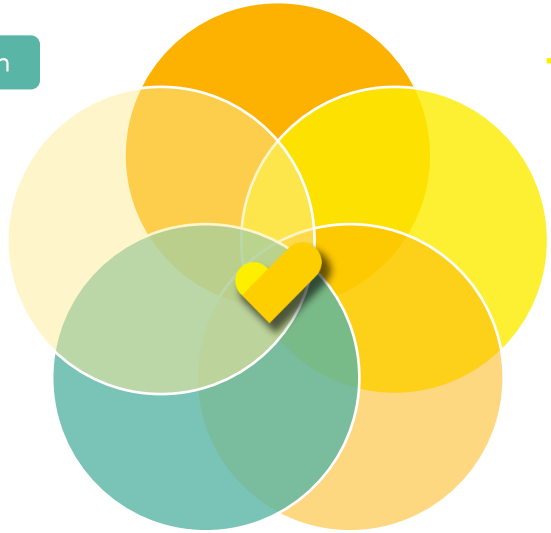
E.g.: *Aggregated amyloid, Alpha synuclein, Tau*

Neurodegeneration

- Chronic infections

E.g.: *HSV*

Infections



- Normal proteins, peptides, hormones validated as targets by mAbs

E.g.: *PCSK9*, *CGRP*, *IL-31*

Cardiovascular

Metabolic

- Previously unattainable or novel combinations

E.g.: *PCSK9/ANGPTL3* for ACVSD; *Myostatin/Activin A* for diabetes/sarcopenia; *RANKL/Sclerostin* for osteoporosis

Oncology

- Inflammatory cells

E.g.: *IgE-bearing B-cells*

Autoimmune

Allergy

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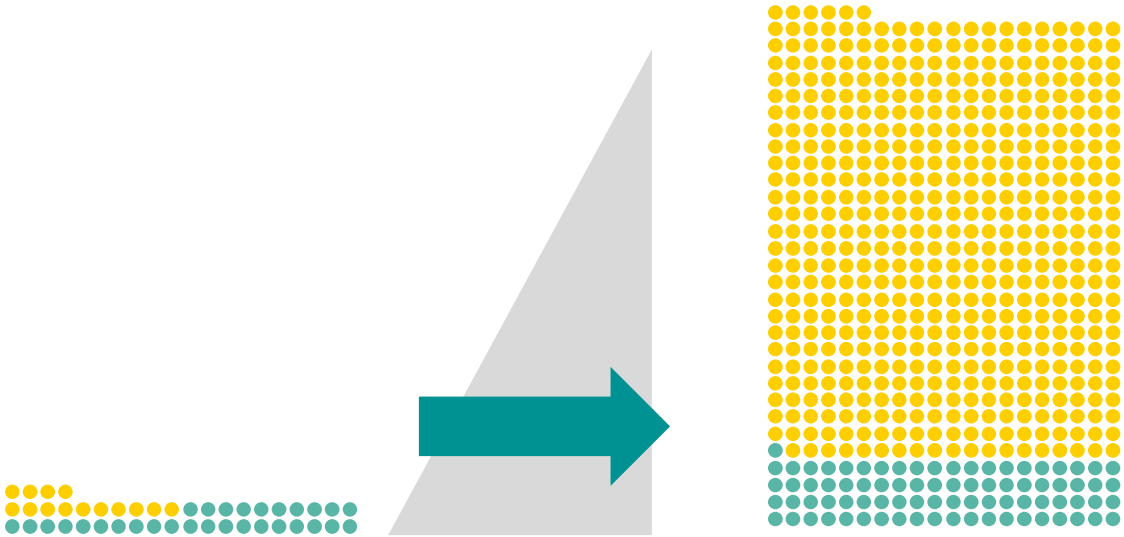
# And grow the pipeline for decades to come



**Current vaccine targets**

30 approved

14 in development

**Potential mAb targets**

Over 80 approved

Over 500 in clinical development

Plus combinations thereof

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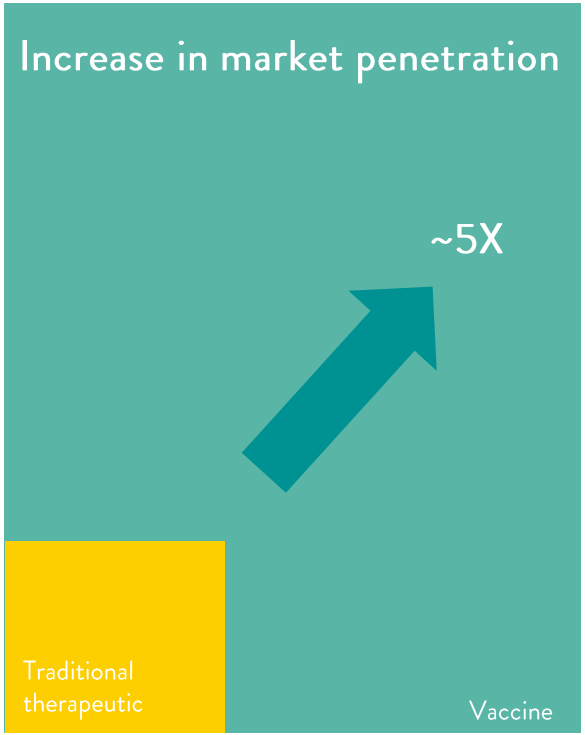
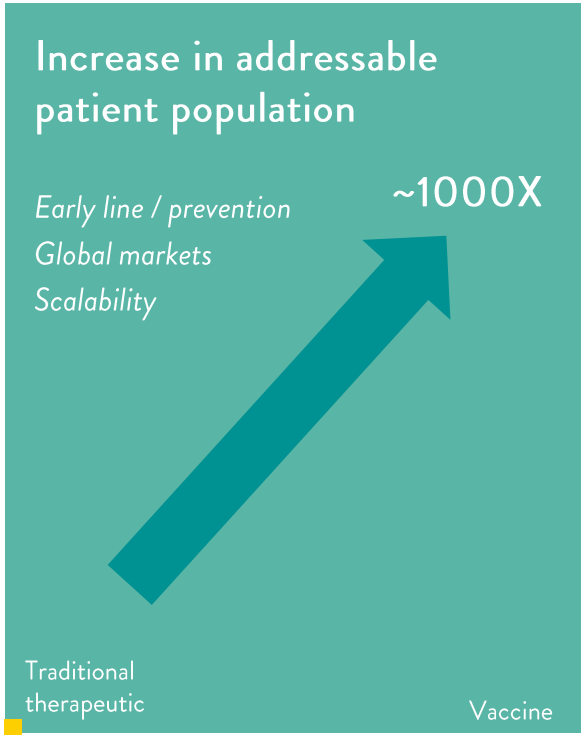
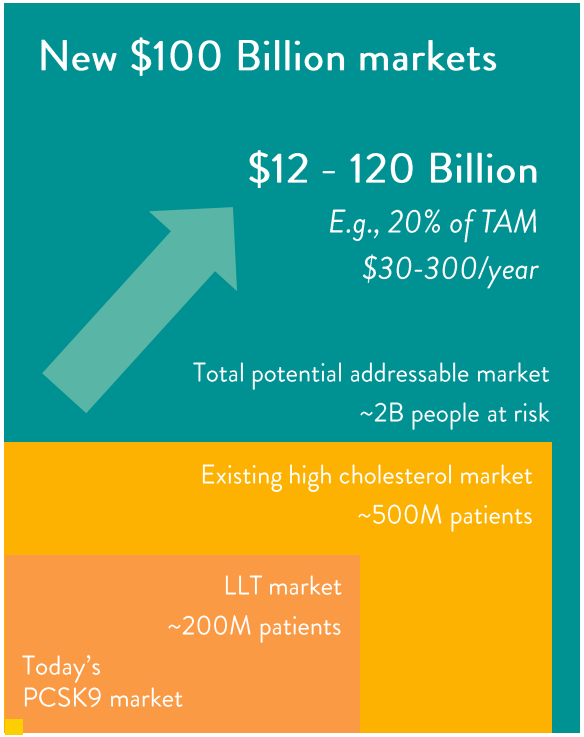
Sources: WHO, NIH, GlobalData. Monoclonal antibody targets do not include discovery/preclinical.

# What could scalable immunotherapeutics for chronic diseases mean?

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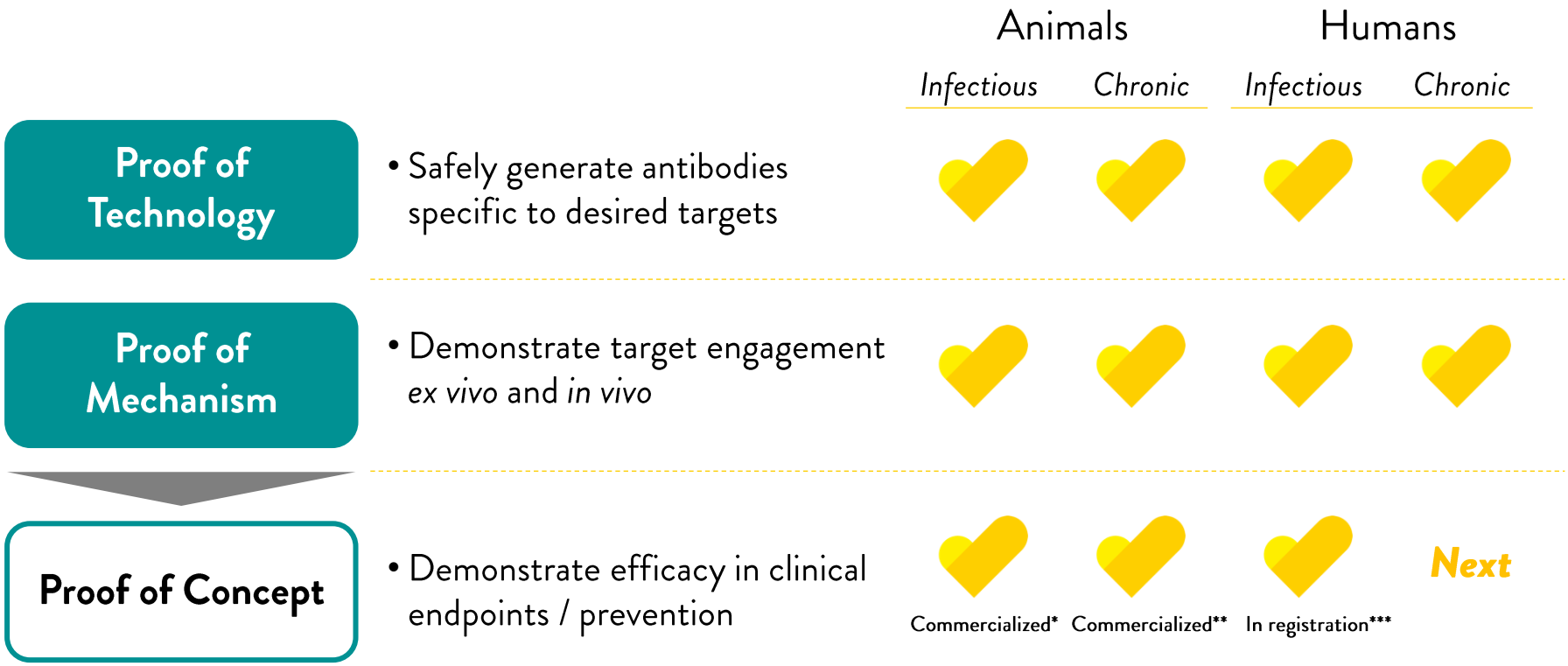
+ Maintenance of margins for investment in further innovation

# Vaxxinity's platform is poised for this next healthcare breakthrough

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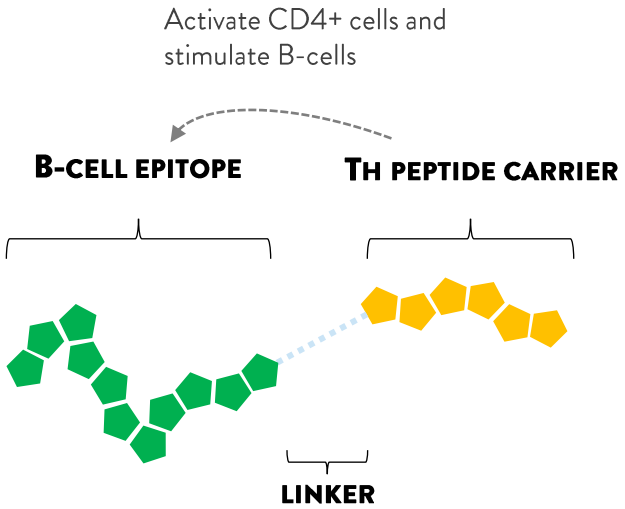
*Foot and mouth disease vaccine; **Anti-LHRH vaccine; ***UB-612 COVID vaccine with MHRA

# Our platform technology

# Our Vaxxine platform enables design of high precision peptide vaccines

| Components |
| --- |
| B-cell epitopes |
| Th peptide carriers |
| Proprietary linker & formulations |




| Advantages |
| --- |
| Breaks immune tolerance |
| Target-specific antibodies |
| Minimal off-target response |
| Synthetic, low-cost, scalable |
| Plug & Play, modular |

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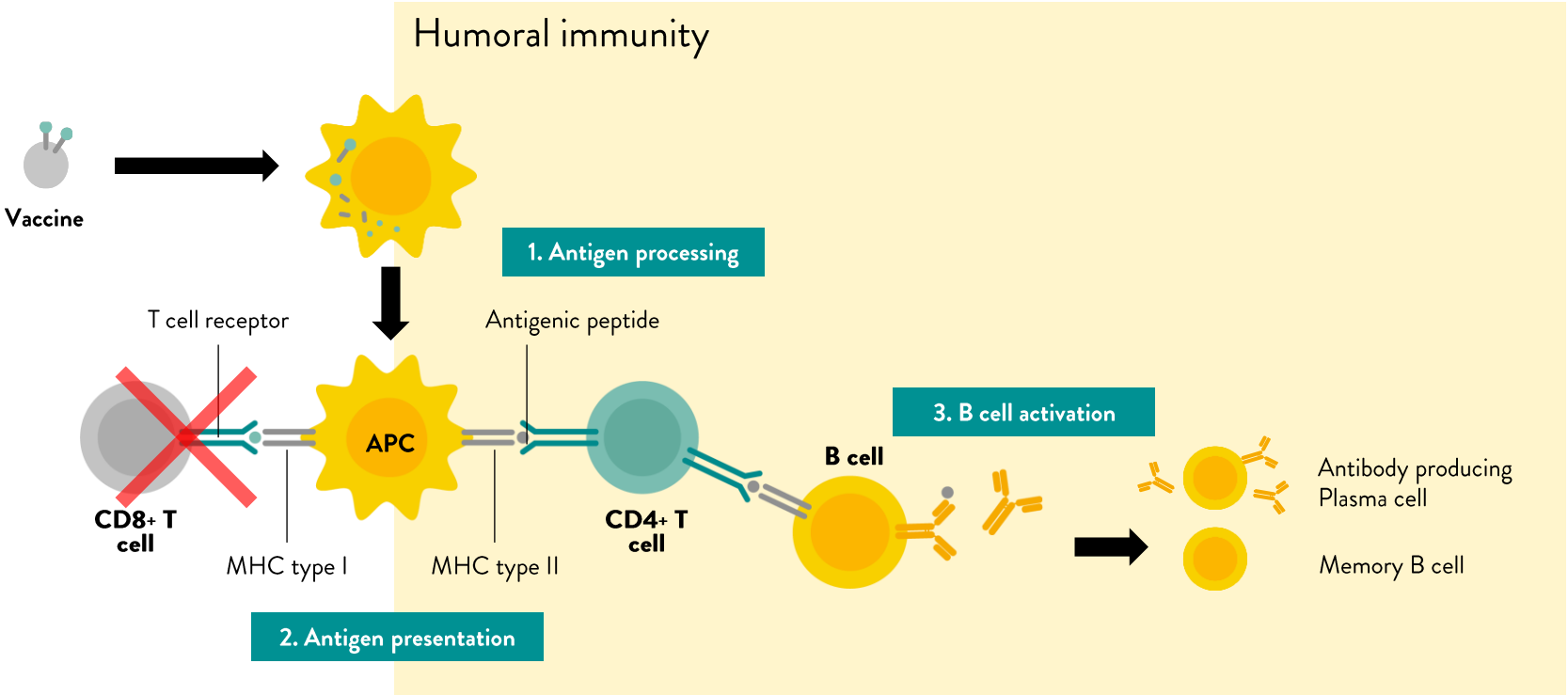
# Our Vaxxines work differently than traditional vaccines

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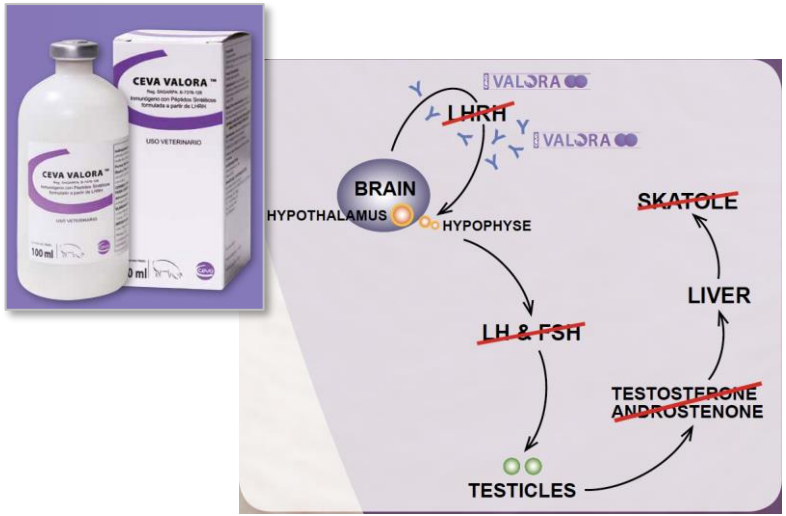
# First Proof of Concept achieved in animal health with high effectiveness and millions of doses commercialized

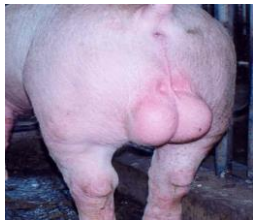
## Anti-LHRH vaccine for immunocastration

### Proof of concept

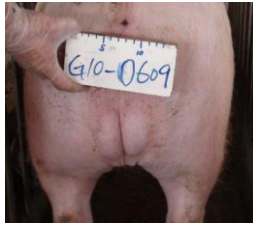
- Breaks immune tolerance against LHRH for swine
- Registered in over a dozen countries
- Commercialized by top 5 animal health company




**Control**



**Treated**

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# We have since translated into a substantial portfolio of clinical data

**5**

investigative VAXXINE medicines in clinical trials

**10**

clinical trials conducted (ongoing and completed)

**10**

repeat doses administered in patients over up to 3 years

**>4,250**

participants dosed

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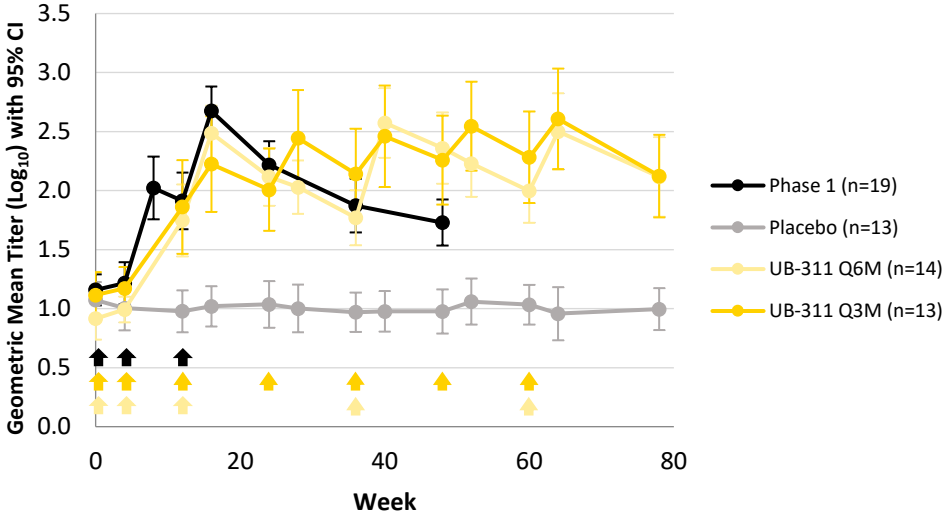
# Our platform consistently breaks immune tolerance to generate antibodies
## *Across 4 clinical programs and over 10 preclinical targets thus far*

### Proof of technology

- 98% patient responder rate
- Antibody concentrations generated comparable to therapeutic mAbs
- **Well-tolerated**, avoiding T-cell inflammation
- **Penetration across BBB*** (~0.2% rate)

**Example: UB-311 Anti-Aβ Antibody Levels (Ph1 and Ph2a)**




Wang et al. *Alzheimer's & Dementia* (2017)
Yu et al. *The Lancet EBioMedicine* (2023)
ADPD 2019 and CTAD 2020

*Demonstrated in non-human primates with UB-311 and humans with UB-312

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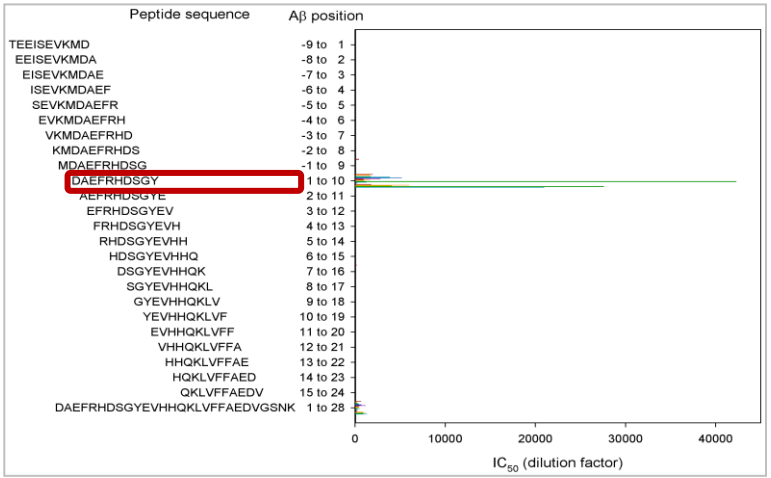
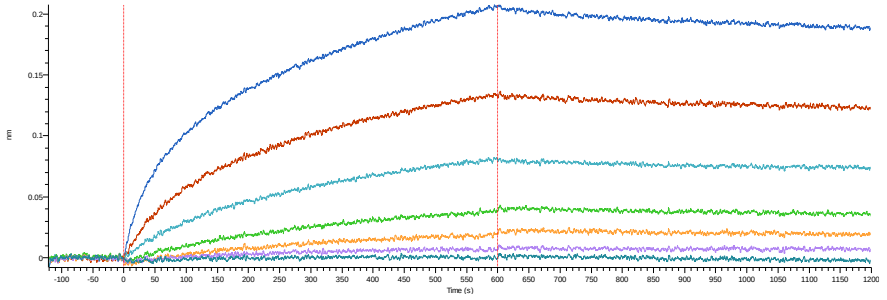
# Vaxxine-induced antibodies are highly specific with strong binding affinity

## High specificity against epitopes




UB-311 Ph1 Patient Serum
Wang et al. *Alzheimer's & Dementia* (2017)

## Strong binding affinity to target




| | $K_D$ (nM) | $k_{on}$ ($M^{-1}s^{-1}$) | $k_{off}$ ($s^{-1}$) |
|---|---|---|---|
| UB-311 IgG fractions | 11.6 | $9.95 \times 10^3$ | $1.15 \times 10^{-4}$ $s^{-1}$ |

UB-311 Ph2a Alzheimer's patient antibodies

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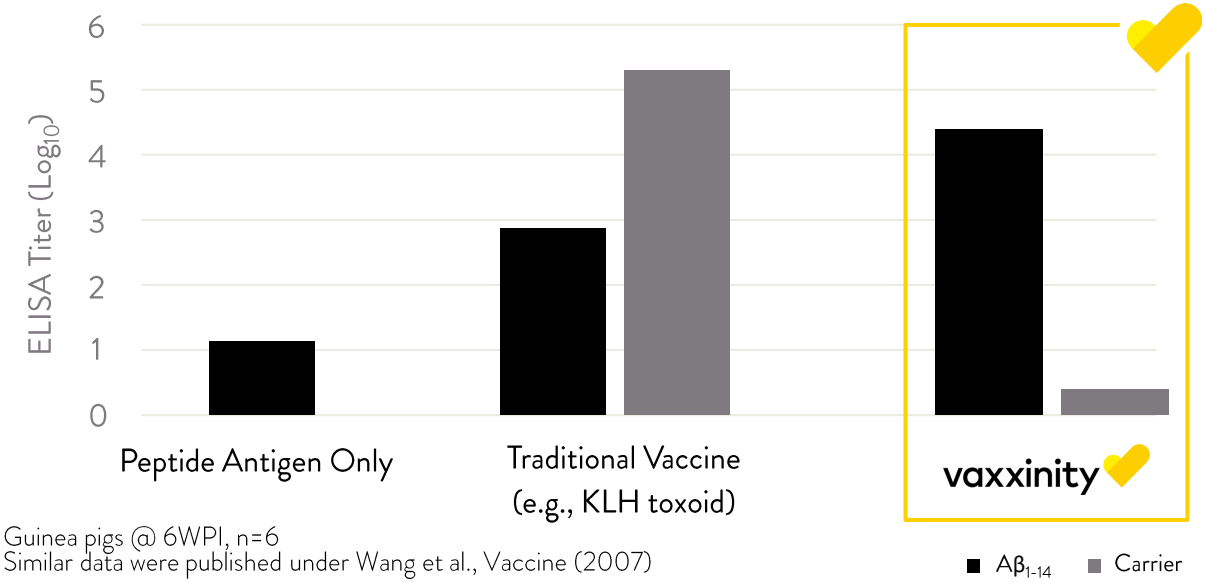
# Unlike traditional vaccines, our platform can break immune tolerance with minimum off-target activity against the carrier…

## Proof of technology

- No other vaccine technology we know of achieves this
- Over 99% of response to desired B-cell epitope rather than carrier, suggesting potential for greater safety

**Example: Immunogenicity against Aβ Peptides and Carrier**



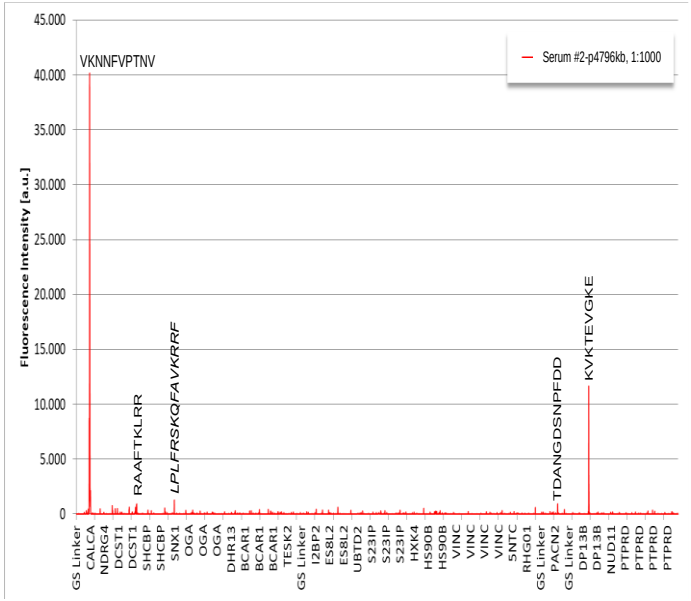

Guinea pigs @ 6WPI, n=6
Similar data were published under Wang et al., Vaccine (2007)

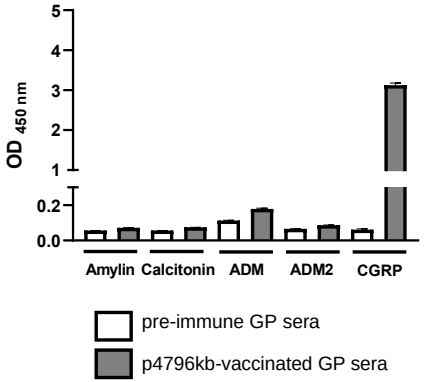
# ...or against other self-proteins

**Example: UB-313 antibody counter-screen against >20,000 proteins**

## Proof of technology

- Initial screen against over 20,000 human proteins
- Additional analysis showed minimum/no binding to others

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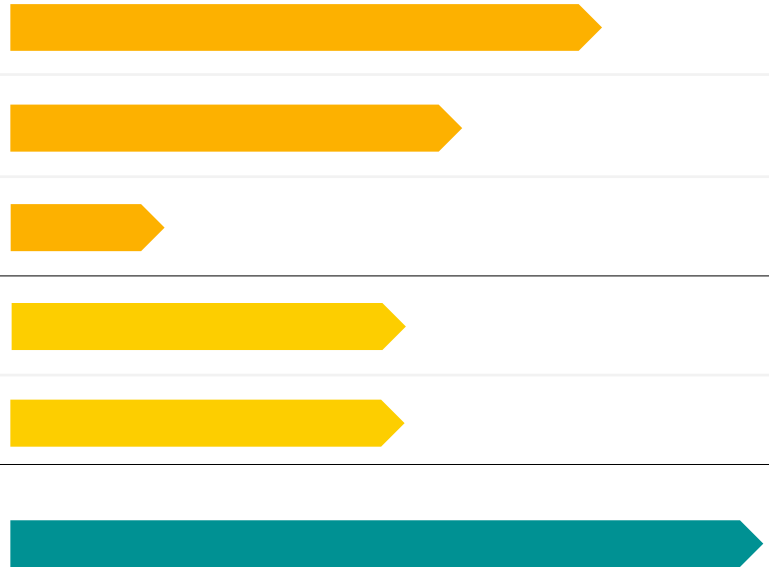
# Our pipeline and what we've shown

- ✓ Proof of technology
- ✓ Proof of mechanism
- ✓ Proof of concept (ID)

# Vaxxinity's pipeline spans multiple therapeutic areas of major unmet need

| | Vaxxine Program (target) | Indications | Preclinical | IND | Ph 1 | Ph 2 | Ph 3 | Next Milestone |
|---|---|---|---|---|---|---|---|---|
| Neurodegeneration | UB-311 (Aβ) | Alzheimer's disease | | | | | | Partner for efficacy study |
| | UB-312 (aSyn) | Parkinson's disease, LBD | | | | | | Full data read-out (1Q24) |
| | VXX-301 (tau) | Alzheimer's disease, tauopathies | | | | | | IND |
| Next wave Chronic | VXX-401 (PCSK9) | Hyper-cholesterolemia | | | | | | Phase 1 read-out |
| | UB-313 (CGRP) | Migraine | | | | | | Dose escalation study |
| Infectious Disease | UB-612 (SARS-CoV-2) | Covid-19 prevention | | | | | | Authorization (MHRA and TGA) |



*Additional undisclosed programs in early drug discovery*

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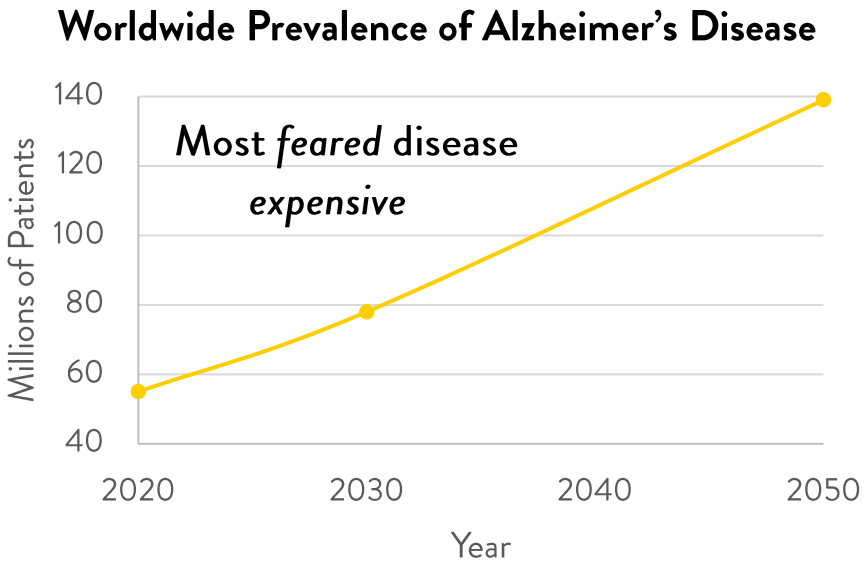
# The Alzheimer's epidemic is unsustainable

## Alzheimer's is doubling every 20 years




## Today's new drugs won't stop the train

- Recently approved disease-modifying mAbs **validate amyloid as key disease driver**
- Analysts estimate less than 0.2% of Alzheimer's patients to be served worldwide
- **Access is severely limited** by cost, manufacturing and infrastructure

**Unmet need: How to treat 100X more people at 10% the cost while maintaining margins?**

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Source: Alzheimer's Disease International, Dementia Statistics

# Potential Best-in-class: UB-311 for Alzheimer's could be the first vaccine to treat and prevent Alzheimer's worldwide

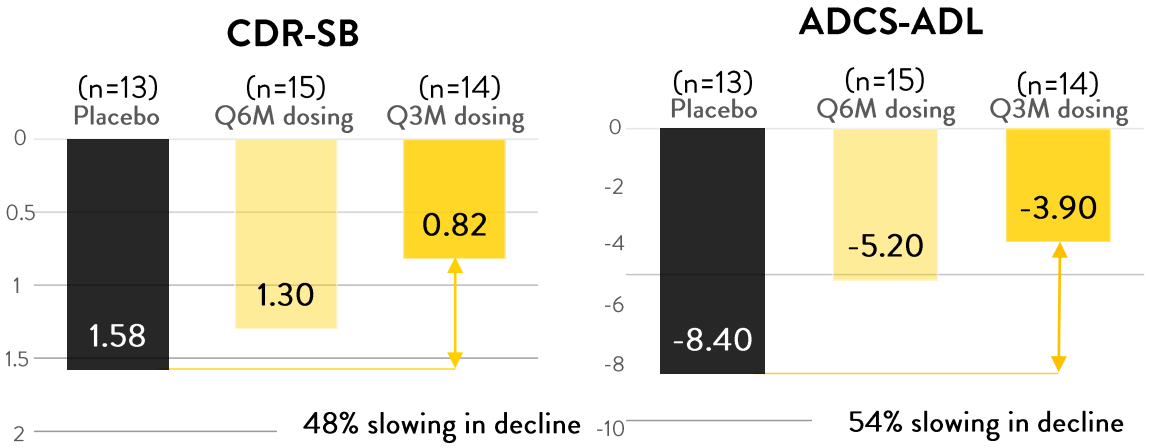
## Proof of technology

- **98% responder rate with high titers**
- **Antibodies cross BBB and bind to toxic Aβ oligomers**
- Demonstrated **well tolerated** safety profile, **no ARIA-E** in Ph2a main study
- Trends of **~50% slowing of cognitive decline** across key measures*

**Status:**

- **Completed Phase 1 and Phase 2a and LTE; FDA Fast Track Designation**
- **Published in The Lancet eBioMedicine (2023), Alzheimer's & Dementia (2017), Vaccine (2007); presented at CTAD (2020, 2018, 2017, 2016), ADPD (2019)**

**UB-311 Directional Slowing of Decline** (Ph2a, baseline to week 78)*

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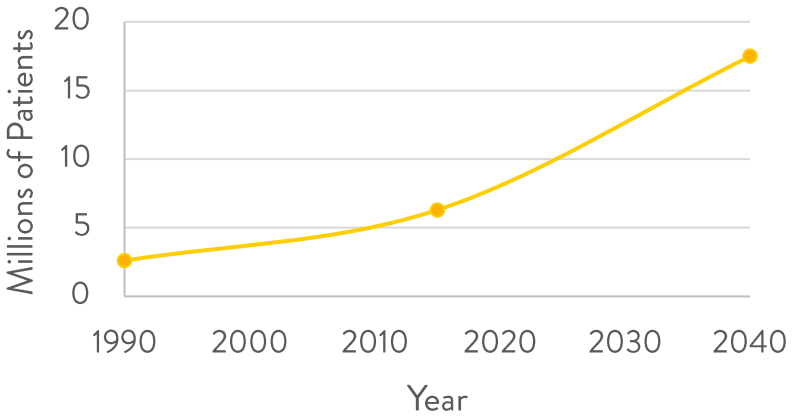
*Ph2a trial not powered for statistical significance

# Parkinson's is the fastest growing neurological disease worldwide

## The Parkinson's Pandemic

### Worldwide Prevalence of Parkinson's Disease




## No Cure or Disease-Modifying Treatment

- Only symptomatic drugs approved
- **Learnings from AD success:**
  - Right species of target
  - Right patient population
  - Right clinical endpoint or impact on surrogate biomarker

**Unmet need: Identify disease-modifying candidate that can impact right biology?**

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Source: Dorsey et al. (2018)

# Potential Best and First-in-class: UB-312 for Parkinson's is first candidate to report reduction in pathological aSyn in patient CSF

## Proof of mechanism of action

- 92% PD patient responder rate
- Antibodies preferentially target aggregated aSyn and penetrate BBB
- Demonstrates target engagement in multiple assays
- First to show reduction in pathological aSyn

**Status:**

- **Phase 1 Part A and B completed; Full dataset with biomarker and efficacy data to be presented at conference (1Q24)**
- **Published in The Lancet (Preprint, 2024), Movement Disorders (2022), Acta Neuropathologica (2022), Alzheimer's Research & Therapy (2020); presented at ADPD (2022), Parkinson's UK (2018)**

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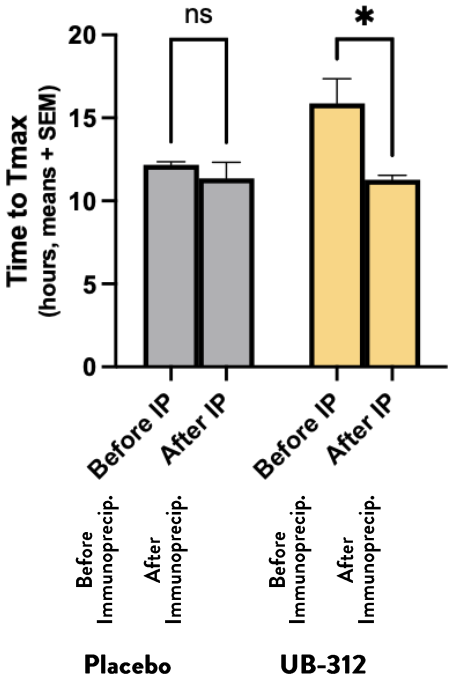
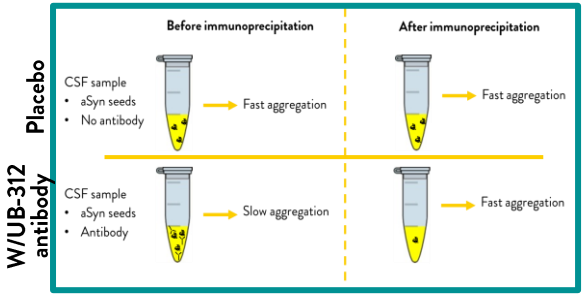
## Target Engagement: UB-312 induced antibodies slow aSyn aggregation in PD patients



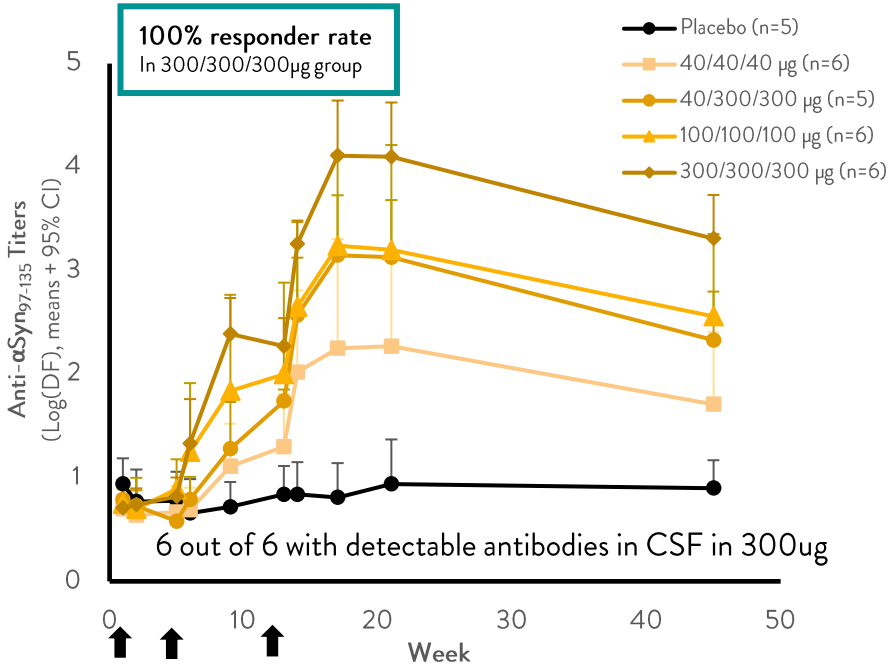




Gray = placebo patient week 17 antibodies (Ph1 Part B); Yellow = UB-312 antibodies week 17 antibodies (Ph1 Part B); CSF seeding assay, additional analyses in progress

Source: Amprion

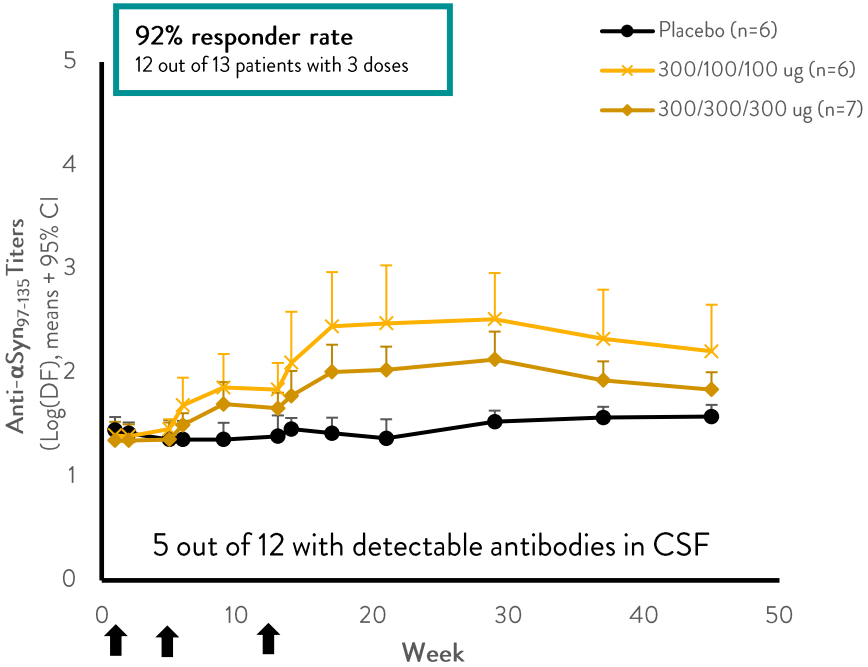
# UB-312 breaks immune tolerance and induces antibodies that cross BBB in healthy volunteers and Parkinson's disease patients

## Anti-aSyn Serum Titers in HV




6 out of 6 subjects who completed 300/300/300µg dosing generated anti-aSyn Ab
Yu et al., *Movement Disorders* (2022)

## Anti-aSyn Serum Titers in PD Patients




12 out of 13 patients who completed dosing with UB-312 generated anti-aSyn Ab.
Source: Vaxxinity

Dosing

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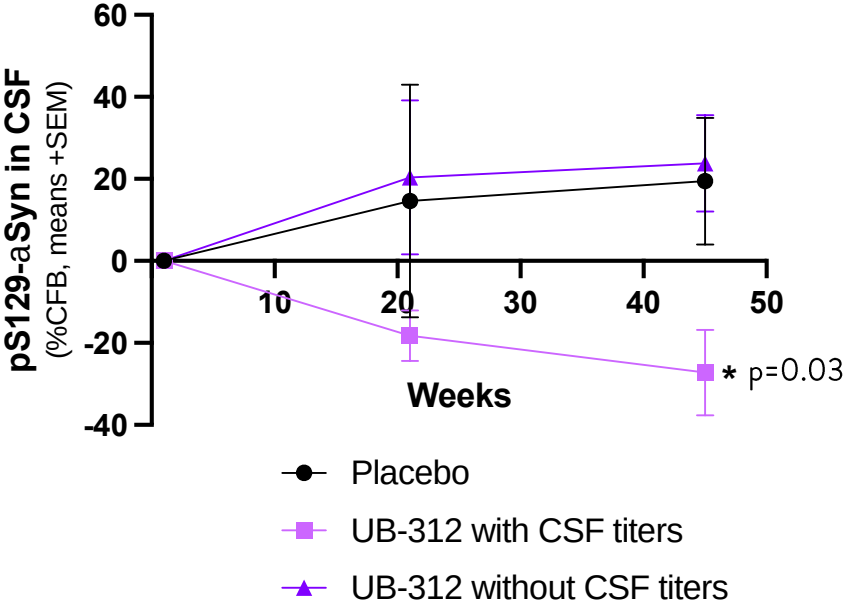
# UB-312 is first candidate to report reduction in pathological aSyn in patient CSF

**Phosphorylated aSyn over time after UB-312 priming regimen only**

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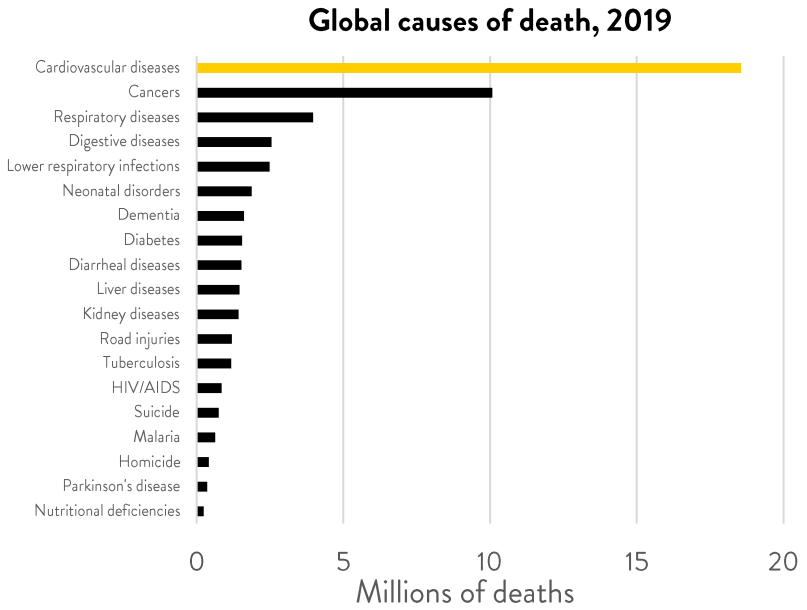
# Cardiovascular disease remains leading killer in world despite effective therapies

## CV disease is top cause of death globally




## Efficacy ≠ Effectiveness

**Statins** are efficacious, but require daily dosing

- Suffer from <30% adherence

**MAbs** are efficacious, but reserved for later line eligibility due to

- High cost
- Low scalability
- Administrative burden

**Unmet need: How to serve 1000X more people and increase patient compliance?**

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Source: Our World in Data (2019)

# VXX-401 for Hypercholesterolemia targeting PCSK9 reduces LDL-C in animals and could do so too in humans

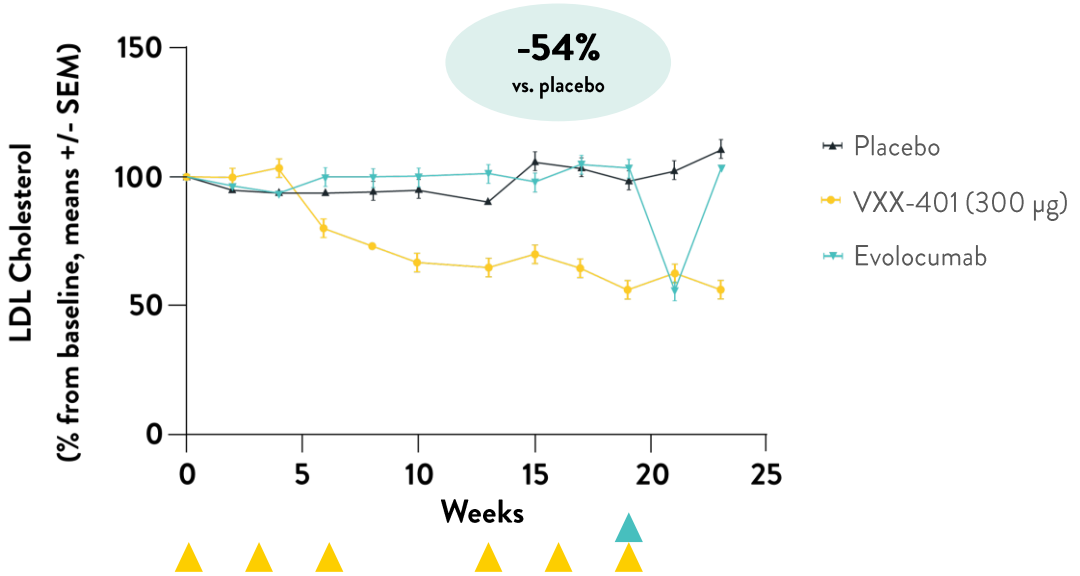
## Proof of concept

- Consistently lowers LDL 30-50% across preclinical species
- High antibody titers across species
- Modality would allow cumulative LDL reduction over long periods of time

**Status:**

- **Phase 1 ongoing; Topline data (mid-2024)**

**VXX-401 lowers LDL-C over time in NHPs**




Cynomolgus monkeys (n = 3 per group) were immunized with a non-optimized formulation of VXX-401 over a 6-week period, then received boosts on weeks 13-19. Immunized NHPs had significantly reduced serum LDL compared to non-immunized NHPs ($p < 0.0001$).

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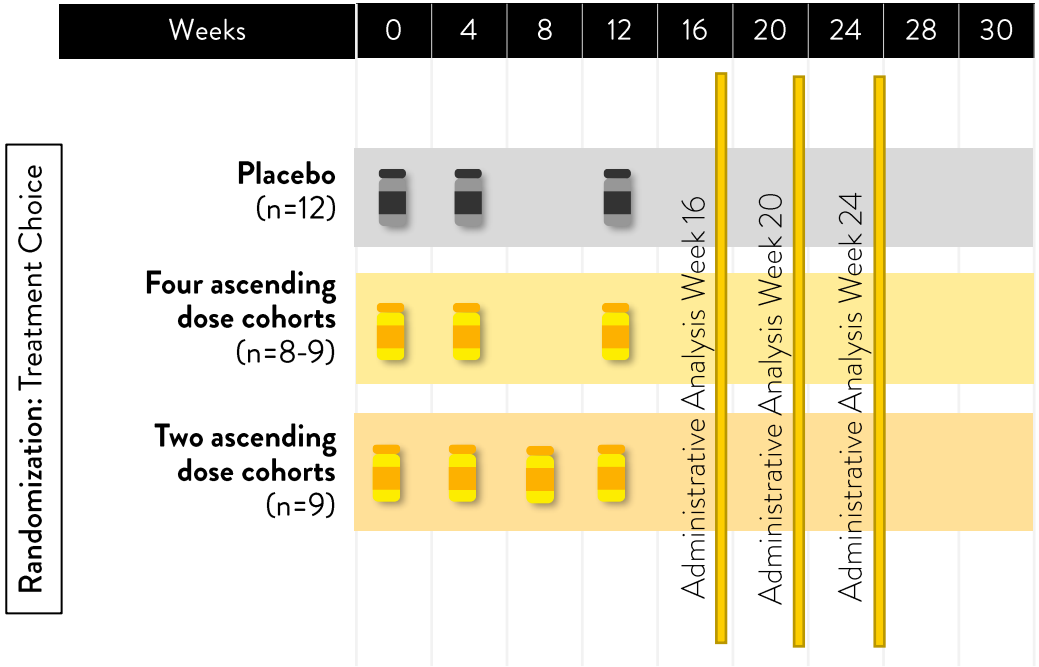
# VXX-401 Phase 1 Study

Healthy Volunteers (LDL-C 2.59-4.89 mmol/L, naïve to statins or with washout of prior statins)




| Study Objectives | |
|---|---|
| Primary | Frequency of AEs<br>Immunogenicity (anti-PCSK9 antibodies)<br>Seroconversion |
| Secondary | % change in LDL-C concentration |

N=48 = Placebo dose = Active vaccine dose

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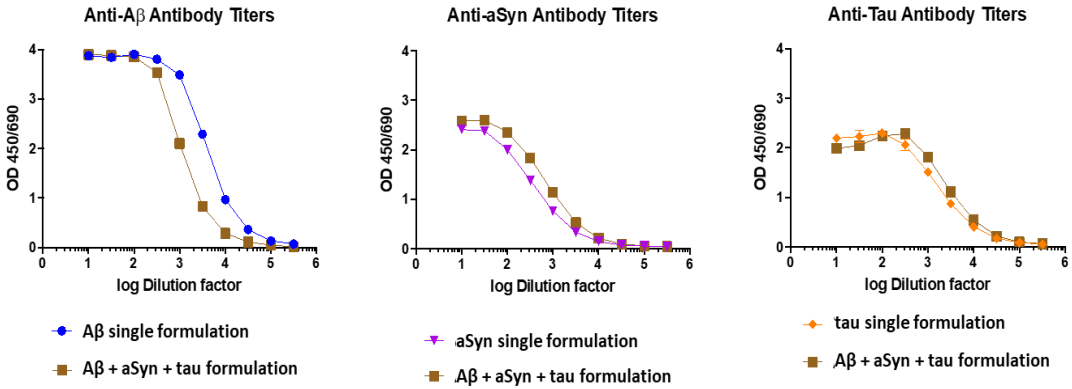
# Aβ-Tau-aSyn Combination: Ability to break tolerance against multiple epitopes

## Proof of technology

- Platform able to break immune tolerance against multiple targets
- Similar titer levels against each target as single-target formulations

**Immunogenicity of Single vs. Multi-Target Formulations**




Guinea pig sera (n=3/group), EIA

# UB-612 for COVID-19 may represent a booster of choice as mRNA alternative

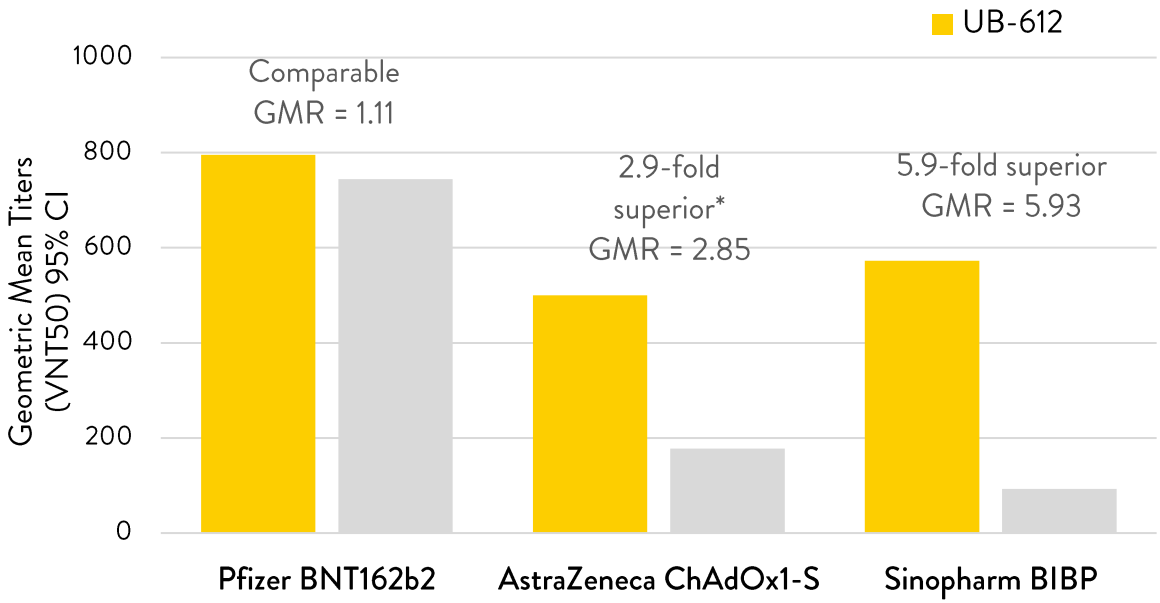
## Proof of concept

- Alternative to mRNA
- Generally well-tolerated with favorable reactogenicity
- Neutralizing antibodies comparable / better than other platforms
- Designed for broad coverage

**Status:**

- **Filed for approval in UK and Australia**

**Phase 3 shows UB-612 boosts better than other platforms**




Ph3 topline results from live SARS-CoV-2 virus neutralization assay 28 days post-injection ^Statistically non-inferior, defined by the lower bound of 95% CI of the geometric mean ratio (GMR) > 0.67;
* p<0.0001 Lower bound GMR CI UB-612 vs. Pfizer against Omicron = 0.94

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# Where next?

# Vaxxinity innovation engine is poised for two clinical read-outs, new preclinical POCs, and to generate revenue with pipeline in 2024

| Program | Next Milestone |
|---|---|
| UB-612 | Approval and commercialization |
| UB-312 | Phase 1 Full Data Read-out (1Q24) |
| VXX-401 | Phase 1 Topline (mid-2024) |
| UB-311 | Active partnership discussions |
| Preclinical | Multi-valent Proof of Concept<br>Platform enhancement |

$43M
*as of 9/30/2023*

Cash + liquid assets

$10M

Grants from
CEPI & MJFF

127M
*as of 9/30/2023*

Common Shares
Outstanding

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Thank You