## Barinthus Biotherapeutics Corporate Presentation

Guiding the Immune System to Cure Disease

March 20, 2024



NASDAQ: BRNS

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## **Company Overview**

Guiding the immune system to cure disease

### Diversified pipeline with anticipated near-term clinical milestones

- 4 programs across infectious diseases, autoimmunity and cancer, with an additional 4 partnered programs.
- **3** Phase 2 readouts expected in Q2 2024.

### **Strong Cash Position**

- Cash of **\$142 million**<sup>1</sup>.
- Outstanding ordinary shares: 38.6 million.
- Estimated cash runway into Q4 2025<sup>1</sup>.
- No debt or outstanding warrants.

### Validated platforms accumulating clinical data

- Proprietary platforms (ChAdOx, MVA, SNAP) designed to drive **focused immune responses**.
- Clinical data generated across multiple indications (HBV infection, HPV infection, prostate cancer, COVID-19).

### **Our Mission**

Advancing the next generation of immunotherapies that lead T cells to gain control over disease and improve patients' lives.



<sup>1</sup>As of December 31, 2023, as reported on Form 10-K on March 20, 2024

## **Proprietary Platforms and Approach**

Creating More Effective Antigen-Specific Immunotherapies Through Innovative Technologies

Platform	Technology	Differentiators	Areas of Focus	Candidates
ChAdOx MVA MVA	<ul> <li><i>ChAdOx</i>: Modified, replication- incompetent simian adenoviral vector.</li> <li><i>MVA</i>: Well-studied, replication- deficient, attenuated Vaccinia virus.</li> </ul>	Induced the highest published magnitude of disease-specific T cells. <sup>1-4</sup> Elicit high magnitude, durable and polyfunctional CD8+ and CD4+ T cell responses. <sup>1-4</sup>	Chronic infections and cancer	VTP-300 (HBV) VTP-200 (HPV) VTP-850 (Prostate cancer)
SNAP	Self-assembled platform co- delivering multiple antigens and immunomodulators: SNAP-Tolerance Immunotherapy (TI) SNAP-Cancer Immunotherapy (CI)	Modular design utilizing self-assembly to co- deliver multiple antigens and immunomodulators. Can be combined with ChAdOx and/or MVA in sequential combination regimens.	Autoimmune diseases and cancer	VTP-1000 (Celiac disease)

SNAP: Self-assembling Nanoparticle based on Amphiphilic Peptides.

<sup>1</sup>Swadling et al (2014) *Transl Med.*<sup>2</sup> Ewer et al (2017) *NEJM.*<sup>3</sup> Moyo et al (2017) *PloS One.*<sup>4</sup> Voysey et al (2023) *Clin. Exp. Immunol.*; Ewer et al (2016) *NEJM*; Ogwang et al (2015) *Sci Transl Med*; Ogwang et al (2013) *PloS One*; Elias et al (2013) *J Immunol*; O'Hara et al (2012) *J Infect Dis*; Ewer et al (2016) Curr Opin Immunol.<sup>5</sup> Esposito et al (2020) *Sci Transl Med*.



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## Diverse Pipeline With Anticipated Near-Term Clinical Milestones

Harnessing the Power of Antigen-Specific Immunotherapies to Treat Infectious Diseases, Autoimmunity and Cancer

Program	Product Candidate*	Therapeutic For	Preclinical	Phase 1	Phase 2	Phase 3	Status/Anticipated Upcoming Milestones
Infectious Disease Programs	VTP-300 ◆ ③	Chronic Hepatitis B Virus (HBV) infection					Phase 2b & Phase 2a interim analysis (Q2 2024)
	VTP-200 ▶ ⊘	Persistent Human Papillomavirus (HPV) infection					Phase 1b/2 final data readout (Q2 2024)
Autoimmune Programs	VTP-1000	Celiac disease					Phase 1 initiation (Q2 2024)
Cancer Programs	VTP-800/850	Prostate cancer					Phase 1/2 futility data (2025)

Data supporting proof-of-concept announced

Near-term proof-of-concept readout

Sexisting human clinical data

ChAdOx + MVA

SNAP-TI



\*Barinthus Bio has worldwide rights for all product candidates. These are estimated timelines only and our pipeline may be subject to change.

## VTP-300 Hepatitis B Virus (HBV) Therapeutic





## HBV Chronic Infection Represents a Large Market Opportunity for VTP-300

There is an urgent need to develop effective therapeutic strategies to cure chronic HBV infection.



### **1.5M** New HBV infections per year.<sup>1</sup>



### **Limitations of Current Treatments**

- Existing therapies typically require chronic treatment.
- NUCs are slow-acting with low cure efficacy.<sup>3</sup>
- Pegylated interferon has significant side effects.<sup>4</sup>
- Less than 10% of patients achieve a functional cure with existing therapies.

HBV: hepatitis B virus; NUCs: Nucleos(t)ide analogs. <sup>1</sup> WHO, <u>Hepatitis B</u>, 2022<sup>, 2</sup> Barinthus Bio, Data on file. <sup>3</sup> Broquetas T and Carrion JA, *Hepat Med*. 2002;14:87-100. <sup>4</sup> Van Zonneveld M, et al, *Aliment Pharmacol Ther*. 2005;21(9):1163-71



## VTP-300 Could be a Critical Component to a Functional Cure Regimen for HBV

VTP-300 is an antigen-specific investigational immunotherapy that could be a critical component to enhancing rates of a functional cure. A functional cure will likely require a combination of agents with complementary mechanisms of action.

#### Approved Investigational Investigational Directly lower viral antigen Inhibit viral Stimulate host immune Hepatitis B surface antigen replication system response burden (HBsAg) Ag-specific immunotherapies RNAi NUCs (VTP-300) Oligonucleotide Capsid & Entry Inhibitors **PD-1** Inhibitors (Investigational) Monoclonal antibodies (mAbs) Immunostimulants (TLR agonists)

### Three potential components to a functional cure

VTP-300 is evaluated in combination with other therapies as a **critical component of a functional cure**.

VTP-300 is designed to engage the host immune system and has been shown to induce sustained HBsAg reduction in Ph2b.



**VTP-300** 

## HBV003 – Phase 2b Study – Currently Enrolling Patients



#### **Inclusion Criteria**

- HBV DNA ≤1,000 IU/mL.
- HBsAg ≤200 IU/mL.
- On NUCs for ≥6 months.

### **Primary Endpoint**

 % participants with a greater than 1 log HBsAg reduction at 6 months after initiation of therapy.

### **Secondary Endpoints**

- Safety: incidence of AEs and SAEs.
- T cell response.

#### HBV003 results will inform treatment dosing regimen

**Group 1:** Mirrors Group 3 in HBV002 to further support response effect observed.

**Group 2:** Assesses if additional dose of MVA-HBV with LD nivolumab at Day 85 further reduces HBsAg.

**Group 3:** Assesses if delaying LD nivolumab until after MVA-HBV is more optimal (plus adds option of 2nd MVA-HBV dose).



## VTP-300 in Combination with Nivolumab Continues to Show Sustained HBsAg Reductions

VTP-300

HBV003 Phase 2b – Preliminary Data<sup>1</sup>

- VTP-300 + nivolumab treatment led to HBsAg reductions in all treatment groups, which were most prominent in patients with HBsAg levels ≤200 IU/mL at screening\*.
- 7 of 9 (78%) participants who reached Day 169 with screening HBsAg below 200 IU/mL were eligible to discontinue NUC therapy.
- 3 participants have discontinued NUC therapy, with **1 retaining undetectable HBsAg 16 weeks post-discontinuation**.



• 31% of patients with an HBsAg <200 IU/mL at Day 1 had >1 log HBsAg reductions vs 2% of patients with HBsAg levels > 200 IU/mL at Day 1.

• At Day 113, 23% of patients had >0.5 log reductions and 9% of patients had >1 log reductions in HBsAg levels.



<sup>1</sup> Preliminary data presented as an oral presentation at AASLD, Q4 2023.

## AB-729-202 – Phase 2a Clinical Collaboration with Arbutus: Study Design



VTP-300

### Imdusiran (RNAi) + VTP-300 +/- Iow-dose nivolumab (N=60)

### Trial expanded in Q4 2022 to include an arm with low-dose nivolumab

#### Patients to discontinue NUCs if eligible



### **Inclusion Criteria**

- HBV DNA ≤20 IU/mL.
- HBsAg ≥100 to <5,000 IU/mL.
- On NUCs for at least 1 year.

- \* Additional MVA/Placebo to be dosed at Week 38, if patients have experienced a  $\geq$ 0.5 log drop in HBsAg from Week 26 to Week 34.
- \*\* Additional MVA+nivo to be dosed at Week 38, if patients have HBsAg ≥10 IU/mL at Week 34.

### **Primary Endpoints**

Safety: incidence of AEs and SAEs.

### **Secondary Endpoints**

- Change in HBsAg concentration from baseline.
- Proportion of participants with a change in HBsAg from baseline meeting response criteria (≥0.5, 1, 2, or 3 log10 reduction).
- Change in HBV DNA, RNA, core-related antigen, HBsAg antibody, HBsAg e-antibody from baseline.



LD: Low-dose

## Imdusiran and VTP-300 Demonstrated Meaningful and Sustained Declines in HBsAg Levels

AB-729-202 Phase 2a - Interim Data<sup>1</sup>

### **Preliminary results:**

- Robust reductions of HBsAg were observed during the imdusiran treatment period, with 33/34 (97%) of subjects <100 IU/mL at the time of VTP-300/placebo administration.
- VTP-300 treatment appeared to contribute to maintaining low HBsAg levels in the early post-treatment period.
- All subjects who have reached Week 48 in Group A (n=5) were eligible to stop NUC therapy and remain off-treatment.\*\*
- HBV-specific T cell IFN-γ production was enhanced in subjects receiving VTP-300 (n=4) vs placebo (n=3).

### Next anticipated readout: Interim data – Q2 2024

<sup>1</sup> Based on interim data analysis presented as a poster by Arbutus Biopharma at AASLD, Q4 2023.
 \*3 subjects have not yet reached VTP-300 dosing period and are excluded from plot
 \*\*As of data being presented at AASLD, Q4 2023.

### Mean HBsAg Change from Baseline by Treatment Group





VTP-300

## VTP-200 Human Papillomavirus (HPV) Therapeutic



## Persistent HPV Infection Remains a Significant Public Health Problem<sup>1</sup>

We are targeting persistent HPV infection – which can lead to precancerous lesions and cervical cancer<sup>1</sup> HPV is the most common sexually transmitted viral infection in the world<sup>1</sup>

Cervical cancer was the 4<sup>th</sup> most common cancer in women globally in 2020.<sup>2</sup> >95% of cervical cancer is caused by HPV.<sup>2</sup>  ~291 million women worldwide are infected with HPV<sup>4</sup>
 >3.6M diagnosed annually with persistent high-risk cervical HPV in US and across 5EU.<sup>6</sup> Cervical cancer in the US<sup>3</sup>:

~4,000 deaths per year even with screening & treatment

~12,000 cases per year

### Cervical cancer worldwide<sup>2</sup>:

**VTP-200** 

- ~342,000 deaths per year
- ~604,000 cases per year

- VTP-200 aims to address high unmet need for patients with persistent HPV infection
- While HPV prophylactic vaccines are effective at preventing infection, there are low vaccination rates exist in many regions of the world and these vaccines do not eliminate existing infections.<sup>1</sup>
- Standard of care is monitoring and excision once high-grade lesions develop.<sup>1</sup>
- Currently no treatment before high-grade lesions develop.1
- People with HPV infections report cancer-related fear, worry over lack of treatment and HPV being a 'ticking time bomb'.<sup>5</sup>





## APOLLO (HPV001) – Phase 1b/2 Study Design

### Lead-in Phase: (N=9)

**Objective: Evaluating VTP-200** 

immunogenicity and safety

Regions

Group A (n=3)

**Group B** (n=3)

Group C (n=3)

### Main Phase\*: VTP-200 (N=99) – Fully Enrolled

Objective: Evaluating safety data, efficacy data, immunogenicity, dose-response

FU	Group	Day 1	Day 29	
UK	1 (n=16) ChAdOx 2 x 10 <sup>9</sup> vp MVA 1 x 10 <sup>7</sup> pfu			
ChAdOx 2 x 10 <sup>8</sup> vp MVA 1 x 10 <sup>7</sup> pfu	2 (n=16)	ChAdOx 2 x 10 <sup>10</sup> vp MVA 1 x 10 <sup>7</sup> pfu		60 of the main
	3 (n=8)	ChAdOx 2 x 10 <sup>8</sup> vp	MVA 1 x 10 <sup>8</sup> pfu	will be part of an
ChAdOx 2 x 10 <sup>9</sup> vp MVA 1 x 10 <sup>7</sup> pfu	4 (n=8)	ChAdOx 2 x 10 <sup>9</sup> vp	MVA 1 x 10 <sup>8</sup> pfu	immunogenicity
ChAdOx 2 x 10 <sup>10</sup> vn	5 (n=16)	ChAdOx 2 x 10 <sup>10</sup> vp	MVA 1 x 10 <sup>8</sup> pfu	Sub-Sludy
MVA 1 x 10 <sup>8</sup> pfu	6 (n=32)	Placebo	Placebo	

### **Inclusion Criteria**

High risk HPV positive for >6 months and lowgrade cervical lesions.

> SAE: serious adverse events. \*All groups open simultaneously Study Reference: NCT04607850

### **Primary Endpoint**

Safety: incidence of AEs and SAEs.

### **Secondary Endpoints**

- Efficacy.
- Dose determination for further studies.

### **Study Outputs**

Efficacy Data: % clearance of high-risk HPV and cervical lesions evaluated at 12 months.





## VTP-200 Demonstrated Favorable Tolerability and T Cell Profile - Interim Analysis

### APOLLO (HPV001):

Phase 1b/2 Interim Data<sup>1</sup>

- VTP-200 was generally well-tolerated. No productrelated grade 3 unsolicited adverse events, and no product-related SAEs.
- Pooled active groups analysis showed:
  - Robust IFNγ responses, with average of >1,000 spot-forming units/10<sup>6</sup>.
  - Strongest T cell responses were observed against the E1, E2 and E6 antigens.
  - Induction of both CD4 and CD8 T cell responses.
- The trial continues as planned to the 12-month primary endpoint.



### Next anticipated readout:

Final data - Q2 2024



**SAE**: serious adverse events.

<sup>1</sup> Data from 58 patients who had reached at least the 6-month time point, immunogenicity results available from a subset of participants who entered the immunogenicity sub-study (N=45). Interim data presented at the International Papillomavirus Conference.

## VTP-1000 Immune Tolerance Program



## Celiac Disease is a Serious Autoimmune Disease with No Effective Treatment Except Strict Gluten-Free Diet

VTP-1000 aims to restore immune balance in a precise, celiac-specific manner.

~1%	of people in Western countries have Celiac Disease. <sup>1</sup>				
▲ 7.5%	increasing incidence per year. <sup>2</sup>				
~17%	Of patients are correctly diagnosed, which is rising with awareness. <sup>3,4</sup>				



VTP-1000 is designed to induce gluten-specific Tregs and reduce gluten-specific Teff cell response.

Current therapeutic approaches including broad immunosuppression do not address underlying disease, can cause severe side effects, and are not curative.

<sup>1</sup> Al-Toma, A., et al. (2019) United European Gastroenterol J. 7(5), 583-613. <sup>2</sup> King, J.A., et al. (2020) Am J Gastroenterol. 115(4), 507-525.

<sup>3</sup> Clinical Gastroenterology and Hepatology 2018; 16:823-36. <sup>4</sup> European Journal of Ped: 2021, 180: 1941-1946.

![](_page_17_Picture_8.jpeg)

**VTP-1000** 

Celiac Disease

## **SNAP-TI Platform – Pre-Clinical Results**

Inducing antigen-specific tolerance to address autoimmune diseases

![](_page_18_Figure_3.jpeg)

<sup>1</sup> Singh. P, et al, Clinical Gastroenterology and Hepatology 2018.
 <sup>2</sup> Unpublished preclinical data, Barinthus Bio, Data on File.

![](_page_18_Figure_5.jpeg)

**MOG**: myelin oligodendrocyte glycoprotein **mTORi**: mechanist target of rapamycin

### **VTP-1000: Tolerance induction in Celiac**

Immunomodulator and antigens co-delivered by **IM injection** in self-assembled SNAP-TI designed to achieve a favorable antigen-specific Treg to Teff ratio.

Next anticipated milestone:

FPFD: Q2 2024

![](_page_18_Picture_11.jpeg)

## VTP-850 Prostate Cancer Immunotherapeutic

![](_page_19_Picture_2.jpeg)

## Prostate Cancer Remains a Health Priority with High Diagnosis and Recurrence Rates

VTP-850 is a next generation ChAdOx-MVA multi-antigen product candidate designed to induce cytotoxic T cells and prevent advancement to metastatic disease.

Prostate cancer is the <b>4th most common</b> <b>cancer</b> diagnosis in the world. <sup>1</sup>	Prostate cancer worldwide <sup>3</sup> :			
<b>1 in 8</b> men will be diagnosed with prostate cancer in their lifetime. <sup>2</sup>	~1.4M	new cases diagnosed.		
<b>20-40%</b> of patients with non-metastatic prostate cancer experience biochemical recurrence after local therapy (e.g., prostatectomy).	~375K	deaths per year.		

VTP-850 is a novel immunotherapy candidate aiming to prevent advanced disease.

- Biochemical recurrence is indicated by rising PSA levels with no evidence of disease on conventional imaging, meaning the disease was not cured by local therapy.<sup>4</sup>
- Treatment options for patients with biochemical recurrence include systemic therapies such as hormonal or chemotherapy, resulting in toxicity and side effects.

**PSA:** Prostate Specific Antigen. Study Reference: NCT05617040

![](_page_20_Picture_8.jpeg)

VTP-850

![](_page_21_Picture_0.jpeg)

### VTP-800 First-Generation Single-Antigen Immunotherapy Showed Meaningful Reduction in PSA

Phase 2a ADVANCE: VTP-800 + Anti-PD-1 in mCRPC

Study in metastatic castration-resistant prostate cancer (mCRPC) patients using ChAdOx-MVA plus nivolumab

VTP-800 antigen: 5T4

Target patient population: 23 mCRPC patients enrolled.

### Efficacy data readouts:

- >50% reduction in PSA compared to baseline was seen in 22% of patients (5/23).
- Historical comparator with a PSA response to anti-PD-1 alone is ~9%.<sup>1</sup>
- 3 patients with PSA response also had measurable tumors and achieved clinical responses.

![](_page_21_Figure_10.jpeg)

![](_page_21_Picture_11.jpeg)

mCRPC: metastatic castration-resistant prostate cancer; PSA: prostate-specific antigen.

<sup>1</sup> Antonarakis, E. et al. Journal of Clinical Oncology 2020

<sup>2</sup> Data courtesy of Prostate Cancer Vaccine Group, Jenner Institute, UO. mCRPC: Metastatic Castrate Resistant Prostate Cancer

## PCA001 – Phase 1/2 Study of VTP-850 Design

Ongoing Phase 1/2 study for Multi-Antigen VTP-850, a Next-Generation Candidate, Futility Data Expected 2025

Phase 1: Lead-in PhaseVTP-850 (N=15-18)Objective: Dose finding for Phase 2, evaluation of safety and immunogenicity.			Phase 2: Main Phase         VTP-850 (N=125)       Objective: Futility analysis, POC, durability of response rate.					
Inclusion CriteriaPrimary En• Hormone sensitive prostate cancer.• Safety: in			incidence of AEs	and SAEs.				
<ul> <li>Biochemical recurrence after definitive local therapy.</li> <li>No metastases by standard radiography.</li> </ul>		<ul> <li>Secondary Endpoints</li> <li>PSA response, durability of PSA response, duration of PSA response, metastasis- survival, time to metastasis, time to start of androgen deprivation therapy.</li> </ul>					nse, metastasis-free herapy.	
* Including 6 participants from Phas received the same dose regimen) h * Dosing dependent on outcome of Study Reference: NCT05617040	se 1. ** If 4 or more of the 25 participants have a PSA response, Stage 2 will be ope Phase 1.	e 1 participants who Iditional participants.	Next anticipate Futility da	ed m ata: 2	ilestone: 2025	BARINTHU		

## Partnered Programs

![](_page_23_Picture_2.jpeg)

## Barinthus Bio's Partnered Pipeline

Program	Product Candidate		Partner	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	Barinthus Bio Rights	Status/Anticipated Upcoming Milestones
Cancer Programs	VTP-600	<b>NSCLC therapeutic</b> in combo. with checkpoint inhibitor + chemo	LUDWIG CANCER RESEARCH CANCER RESEARCH UK						Worldwide (76% of Sub.)	Phase 1/2a ongoing
	⊘ ● VTP-500	MERS	UNIVERSITY OF OXFORD CEPI						Worldwide	Initiation of Phase 2
Prophylactic Programs	<b>VTP-400</b>	Zoster	🎸 CanSinoBIO						Worldwide (excl. China)	Phase 1 ongoing
	⊘ ● VTP-900	COVID-19 Coronavirus	AstraZeneca	VAXZEVRIA	A®, COVISHI	ELD™			Licensed by OUI to AZ	Fully approved in EMA/UK

![](_page_24_Picture_2.jpeg)

ChAdOx only

ChAdOx ± MVA

![](_page_24_Picture_5.jpeg)

## **Company Highlights**

![](_page_25_Picture_2.jpeg)

## **Financial Overview and Catalysts**

Guiding the immune system to cure disease

### **Current cash position**

 $142 \text{ million}^1$  as of December 31, 2023.

No debt or outstanding warrants.

Estimated cash runway into Q4 2025<sup>1</sup>.

### Expected near-term catalysts<sup>2</sup>

Q2 2024 VTP-200 (HPV): Phase 1b/2 APOLLO (HPV001) final safety, efficacy and immunogenicity data

VTP-1000 (Celiac): Phase 1 GLU001 FPFV

**VTP-300 (HBV)**: Phase 2b HBV003 and Phase 2a AB-729-202 interim analysis data

![](_page_26_Picture_10.jpeg)

## **Investment Highlights**

![](_page_27_Picture_1.jpeg)

**Proprietary platforms** (ChAdOx, MVA, SNAP) designed to drive powerful immune responses in therapeutic and prophylactic settings.

![](_page_27_Picture_3.jpeg)

**Pipeline of 5 programs** in infectious diseases, autoimmunity and cancer

![](_page_27_Picture_5.jpeg)

**Clinical data** in HBV, HPV, prostate cancer and the Oxford-AstraZeneca COVID-19 vaccine.

![](_page_27_Picture_7.jpeg)

**Multiple anticipated near-term data readouts** and clinical trial initiations from three Phase 2 programs and two Phase 1 programs.

![](_page_27_Picture_9.jpeg)

Expanding into autoimmunity with targeted immunotherapies in high unmet need areas with no current treatment, such as Celiac disease.

![](_page_27_Picture_11.jpeg)

**Established partnerships** in **4 programs** with leading institutions and biotech companies.

![](_page_27_Picture_13.jpeg)

# Guiding the Immune System to Cure Disease

Thank You

![](_page_28_Picture_2.jpeg)