

**VBI**  
VACCINES

ACTIVATING THE POWER WITHIN

# Development of eVLP Platform for Viral Associated Cancers

World Vaccine & Immunotherapy Congress 2021

# Forward-Looking Statements

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*Certain statements in this presentation that are forward-looking and not statements of historical fact are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and are forward-looking information within the meaning of Canadian securities laws (collectively “forward-looking statements”). The Company cautions that such statements involve risks and uncertainties that may materially affect the Company’s results of operations. Such forward-looking statements are based on the beliefs of management as well as assumptions made by and information currently available to management. Actual results could differ materially from those contemplated by the forward-looking statements as a result of certain factors, including but not limited to, the impact of general economic, industry or political conditions in the United States or internationally; the impact of the ongoing COVID-19 pandemic on our clinical studies, manufacturing, business plan, and the global economy; the ability to successfully manufacture and commercialize PreHevbrio; the ability to establish that potential products are efficacious or safe in preclinical or clinical trials; the ability to establish or maintain collaborations on the development of pipeline candidates and the commercialization of PreHevbrio; the ability to obtain appropriate or necessary regulatory approvals to market potential products; the ability to obtain future funding for developmental products and working capital and to obtain such funding on commercially reasonable terms; the Company’s ability to manufacture product candidates on a commercial scale or in collaborations with third parties; changes in the size and nature of competitors; the ability to retain key executives and scientists; and the ability to secure and enforce legal rights related to the Company’s products. A discussion of these and other factors, including risks and uncertainties with respect to the Company, is set forth in the Company’s filings with the SEC and the Canadian securities authorities, including its Annual Report on Form 10-K filed with the SEC on March 2, 2021, and filed with the Canadian security authorities at [sedar.com](https://www.sedar.com) on March 2, 2021, as may be supplemented or amended by the Company’s Quarterly Reports on Form 10-Q. Given these risks, uncertainties and factors, you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. All such forward-looking statements made herein are based on our current expectations and we undertake no duty or obligation to update or revise any forward-looking statements for any reason, except as required by law.*

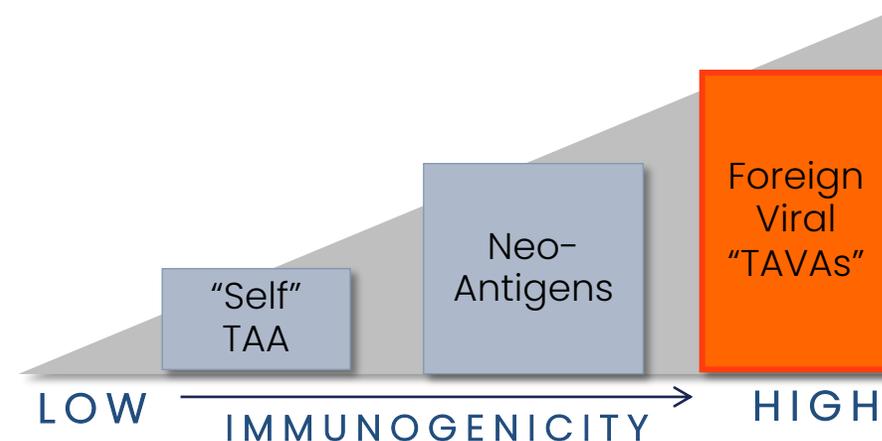
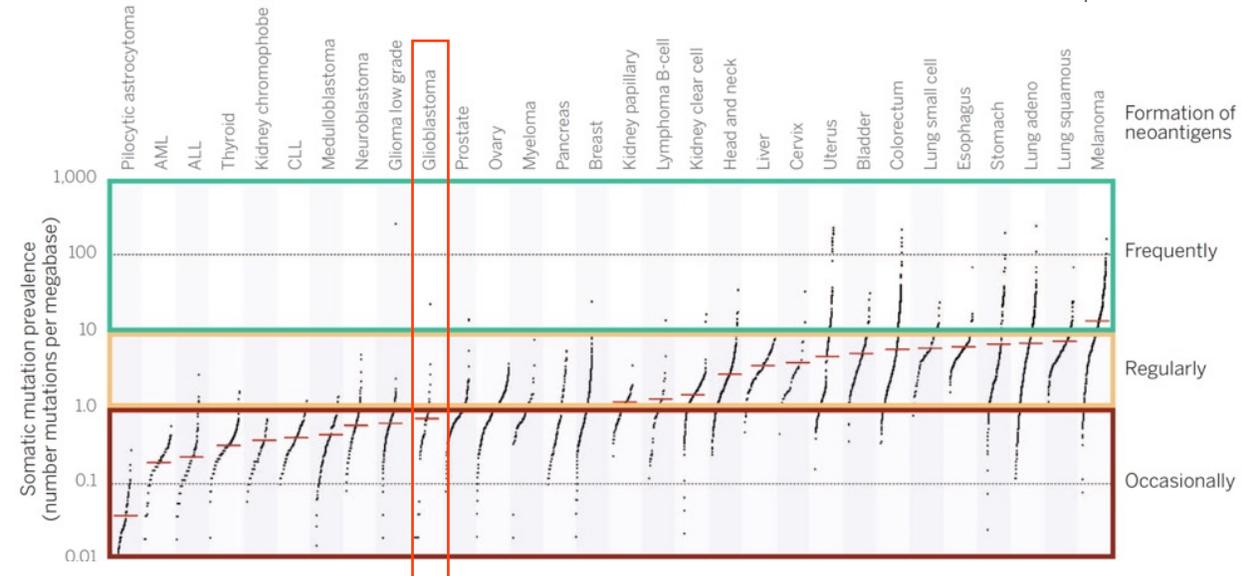


# The Immuno-Oncology Renaissance Depends on an Ability to Activate Anti-Tumor Immunity via Appropriate Antigen Selection

## Historic Context of Cancer Vaccines

- Historically, cancer vaccines have consisted of weakly immunogenic “self” tumor associated antigens (TAA)
  - Central tolerance naturally limits potent responses to “self” TAA
- PD-1 & CTLA-4 blockade success explained by mutation frequency – “neoantigens”
  - Occur in frequently mutating/inflamed/“hot” tumors
  - Enhance immunogenicity in the context of PD-1 or CTLA-4 mAb blockade
- Foreign viral antigens are inherently immunogenic
  - Our body has large repertoires of pre-existing anti-viral T cells (e.g. against CMV, EBV)
  - Opportunity for off-the-shelf therapy
- Tumor-associated viral antigens (“TAVA”) make an ideal antigenic target*

Schumacher & Schrieber, Science, April 2015



# Evidence for Cytomegalovirus (CMV) as a Target Antigen in GBM (1)

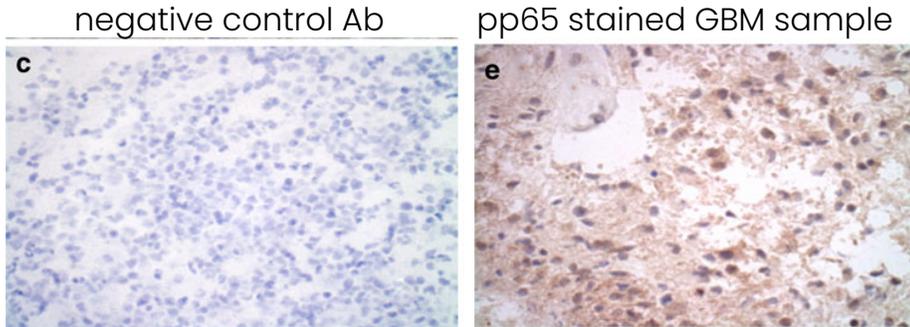
Multiple labs have confirmed presence of CMV antigens in GBM tumor samples but NOT in adjacent healthy tissue

- Cobbs CS (2002)
  - Immunohistochemical (IHC) staining with CMV pp65 antibody confirmed expression in 22/22 GBM tumor samples
  - No CMV expression in normal brain tissue (n=5), stroke tissue (n=4), and brain tissue from Alzheimer's subjects (n=3)
  - *In situ* hybridization (ISH) with CMV-specific probes confirmed reactivity in 8/8 GBM samples but no reactivity in normal brain tissue (n=4), stroke tissue (n=1) or Alzheimer's brain tissue (n=2)
- Mitchell DA (2007)
  - IHC staining with CMV IE-1 antibody confirmed expression in 42/45 GBM tumor samples with no expression in surrounding non-tumor brain tissue
  - IHC staining with CMV pp65 antibody confirmed expression in 30/33 GBM tumor samples but no adjacent areas of normal brain
  - ISH with CMV IE1 probe confirmed reactivity in 16/16 GBM samples but not to blood vessels or normal brain



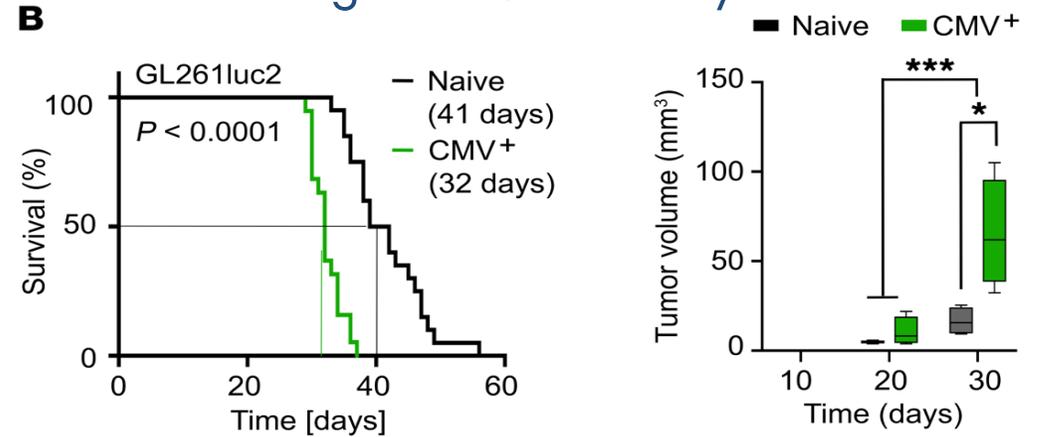
# Evidence for CMV as a Target Antigen in GBM (2)

## Immuno-histochemical Staining of CMV in GBM Samples



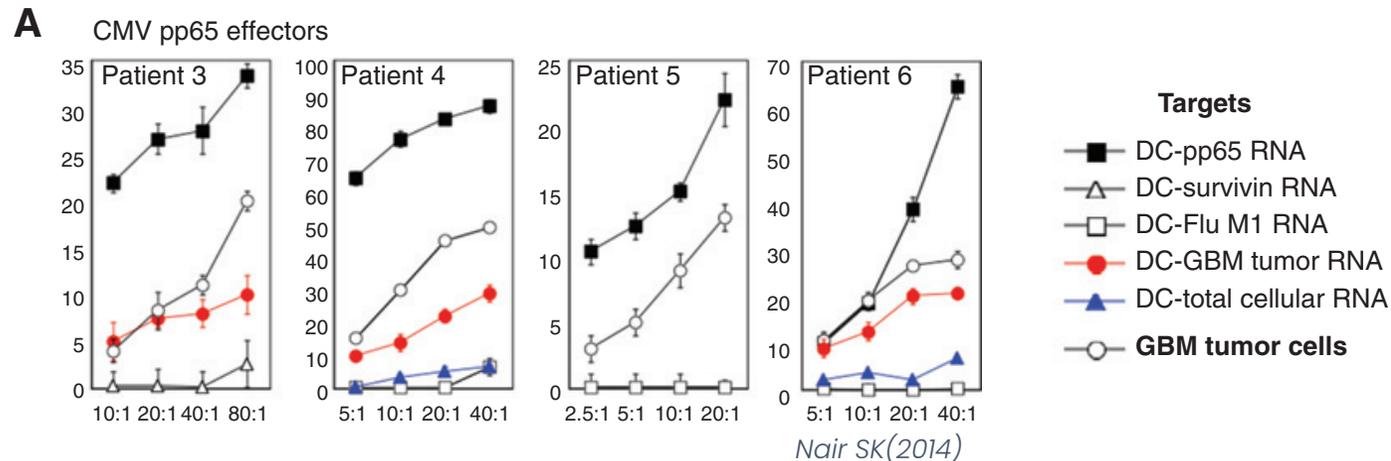
Lucas KG(2011)

## Perinatal infection of mice with MCMV enhances tumor growth & mortality



Krenzlin H (2020)

## Primary GBM Tumors Present Antigens Recognized by CMV Specific T-cells



Nair SK(2014)



# Broad Clinical Evidence Supports CMV as an Immunotherapeutic Target in GBM

- **Prins RM (2008)** – Autologous, GBM tumor lysate DC vaccine
  - Single imzn. increased CMV pp65-specific CD8+ T cells from 0.2% to 4.4%
- **Crough T (2012)** – Single patient receiving 4 infusions of autologous CMV-specific T-cells
  - MRI revealed improvement with stable disease reported for 17 months
- **Schuessler A (2014)** – 10 patients receiving 3-4 infusions of autologous CMV-specific T-cells
  - 10 recurrent GBM pts, 3-4 infusions of autologous CMV-specific T cells
  - Achieved median OS of 403 days and only minor adverse events
- **Mitchell DA (2015)** – CMV-specific DC vaccine with tetanus pre-conditioning
  - OS (>36.6 months) vs. control cohort with median OS of 18.5 months
- **Batich K (2017)** – CMV-specific DC vaccine with GM-CSF & Temozolomide
  - OS increased (>41.1 months) vs historic control
- **Smith C (2020)** – Adoptive CMV-specific T cell therapy of patients with primary GBM
  - Improved overall survival when given prior to recurrence



# CMV Antigens are Present in Multiple Solid Tumors – An Ideal Target

CMV's immunomodulatory properties promote disease progression but its presence provides an opportunity for vaccine-induced tumor targeting & productive inflammation

Potential Application to Multiple Cancers



## CNS Cancers

### Glioblastoma

- Over 95% CMV+
- Key References:
  - Cobbs 2002, 2013
  - Lucas KG 2011
  - Nair SK 2014
  - Batich K 2017
  - Penas-Prado 2018

### Other Brain Tumors

- Wolmer-Solberg N (2013) Int J Cancer
- Baryawno N (2011) J Clin Invest
- Libard S (2014) PLoS ONE

## Other Solid Tumors

### Breast Cancer

- Over 90% CMV+
- Key References:
  - Pasquereau (2017) Open J Virol
  - Herbein (2014) Frontiers Oncol
  - Taher C (2013) J Clin Virol
  - B Cox (2010) BJC
  - Harkins LE (2010) Herpesviridae

### Others Requiring Analysis

- CRC, Prostate
- Prevalence typically ~50% (higher than standard TAAs)



# VBI's Cancer Vaccine Approach is Differentiated from Past Attempts

## Weaknesses of Past Cancer Vaccines

Lack of Inherent Potency

Lack of Balanced Immunity

Lack of Breadth

Poorly Immunogenic Delivery

## The VBI Approach

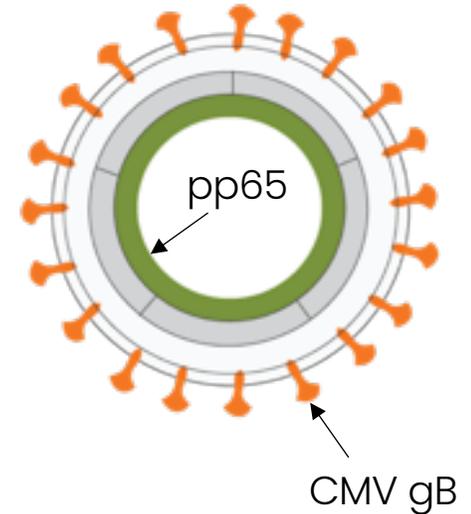
Target CMV+ tumors, where 'anti-viral' immunogenicity dwarfs 'anti-self'

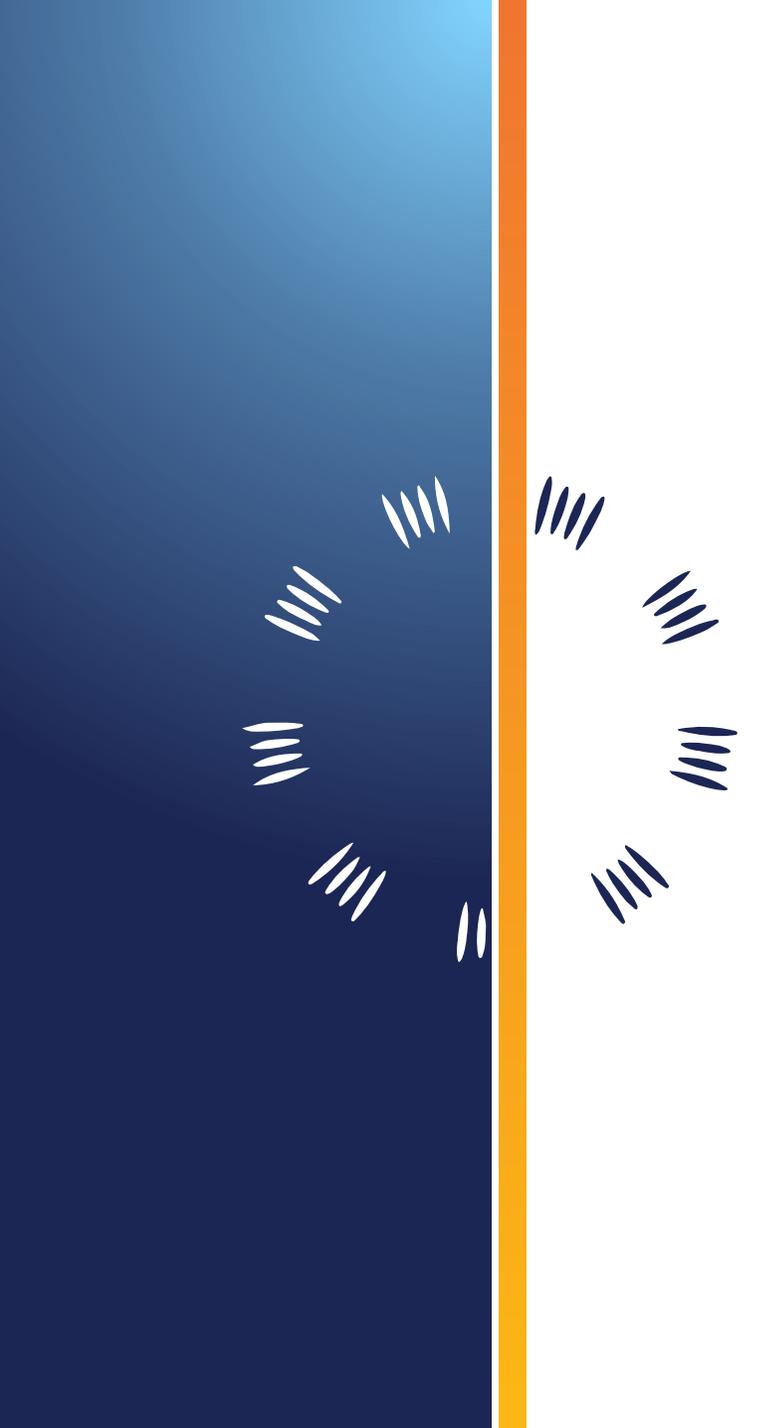
VBI induces both CD4+ and CD8+ immunity

Both gB & pp65 are "full length" to provide multiplicity of epitopes

eVLPs are naturally presented to DCs and stimulate innate and adaptive immunity

## VBI-1901





**VBI-1901:  
Ongoing Phase I/II Trial in rGBM**

# GBM Phase I/IIa Clinical Study Design

Two-part, multi-center, open-label, dose-escalation study of VBI-1901 in patients with recurrent glioblastoma (GBM)

## Phase I (Part A) : Dose-Escalation Phase

*Patient population :*

Recurrent GBM (any # of recurrences)

Study Arm 3:  
High Dose – 10.0µg + GM-CSF

N=6

Enrollment completed December 2018

VS.

Study Arm 2:  
Intermediate Dose – 2.0µg + GM-CSF

N=6

Enrollment completed September 2018

VS.

Study Arm 1:  
Low Dose – 0.4µg + GM-CSF

N=6

Enrollment completed April 2018

## Phase IIa (Part B) : Extension Phase

*Patient population :*

First Recurrent GBM

Study Arm 1:  
10.0µg + GM-CSF

N=10

VS.

Study Arm 2:  
10.0µg + GSK's AS01<sub>B</sub> adjuvant system

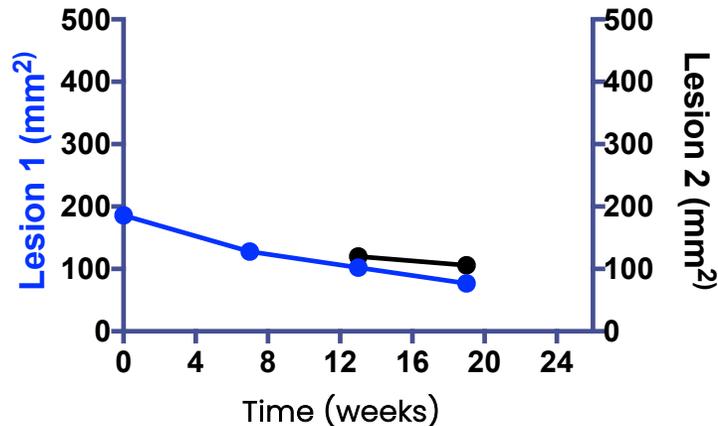
N=10



# Encouraging Tumor Responses & Survival Benefit Observed in Phase 1 (Part A)

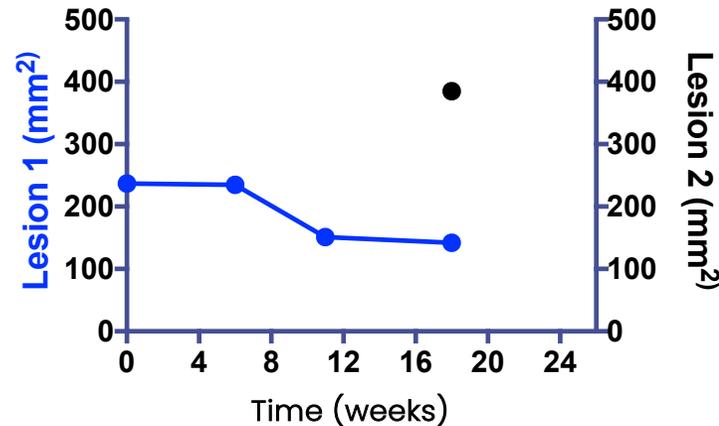
Exemplar Tumor Responses in Subjects Immunized Monthly at Highest Dose Level

Patient 03-006



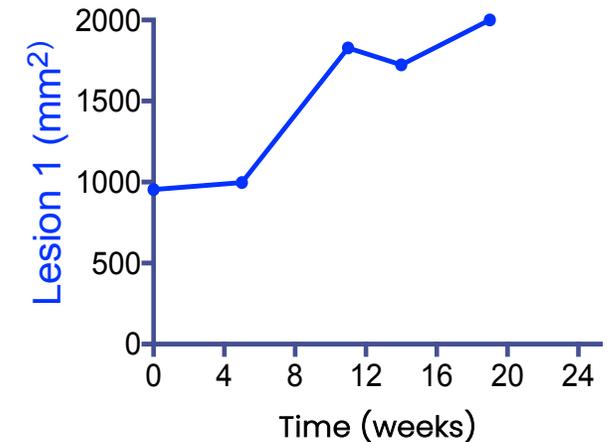
- ~60% reduction in primary tumor
- New tumor (black) prevented PR designation

Patient 03-004



- >50% reduction in primary tumor
- New tumor (black) prevented PR designation

Patient 03-003



- Presumed immune infiltration into tumor (pseudoprogression)



# VBI-1901 Demonstrated Excellent Safety & Promising Immunogenicity and Tumor Impact

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## Phase I (Part A) Summary

### Vaccine Immunotherapeutic Candidate Safe & Well Tolerated

- No vaccine-associated SAEs
- No evidence for vaccine-induced cerebral edema

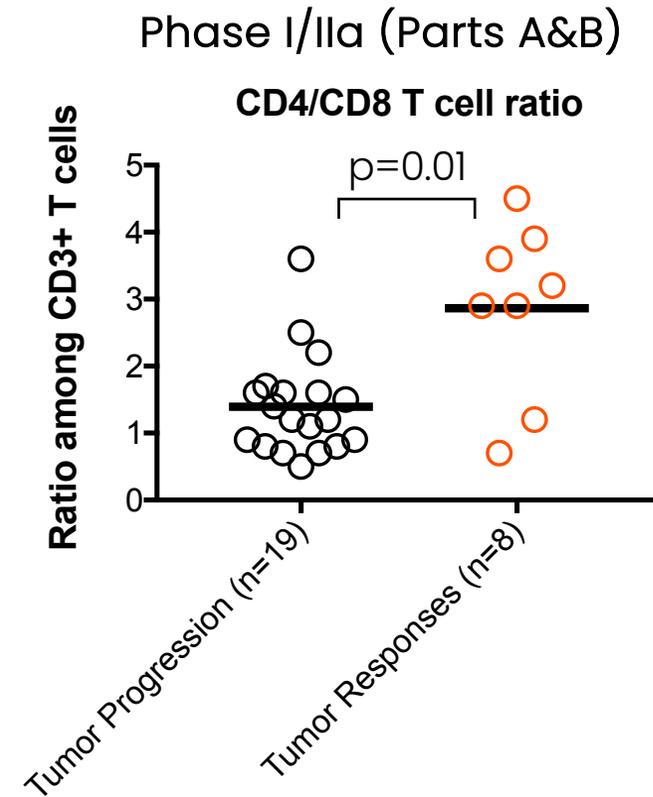
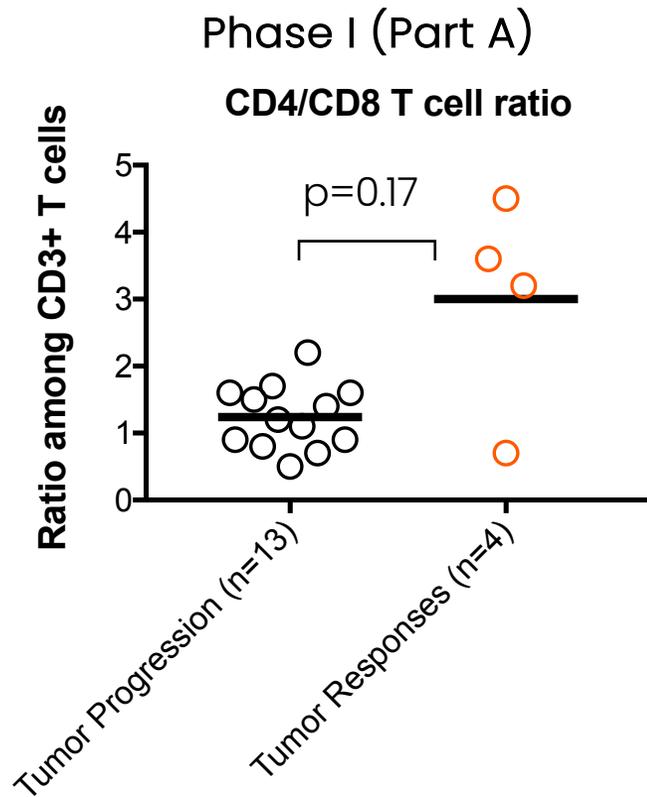
### High Dose Selected for Phase 2a (Part B)

- 3/6 patients in the high dose cohort had evidence of stable disease by MRI compared to 1/6 and 0/6 patients in the low and intermediate dose cohorts



# Can a Baseline Biomarker Be Identified Associated With Those Patients Responding to VBI-1901 Treatment?

Baseline CD4/CD8 T cell ratio captures immunological fitness of patient which enables response to VBI-1901+GM-CSF



## Part A of Trial

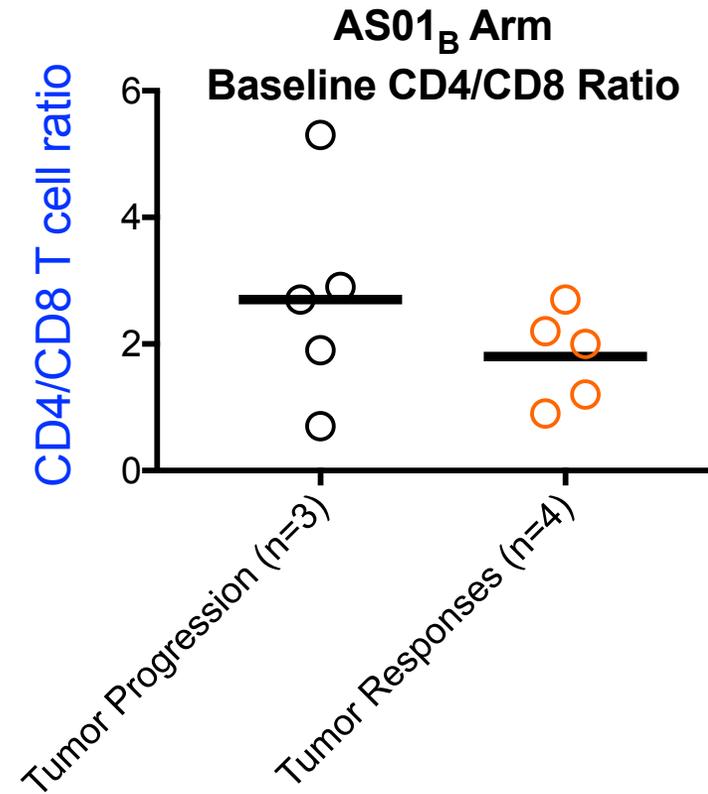
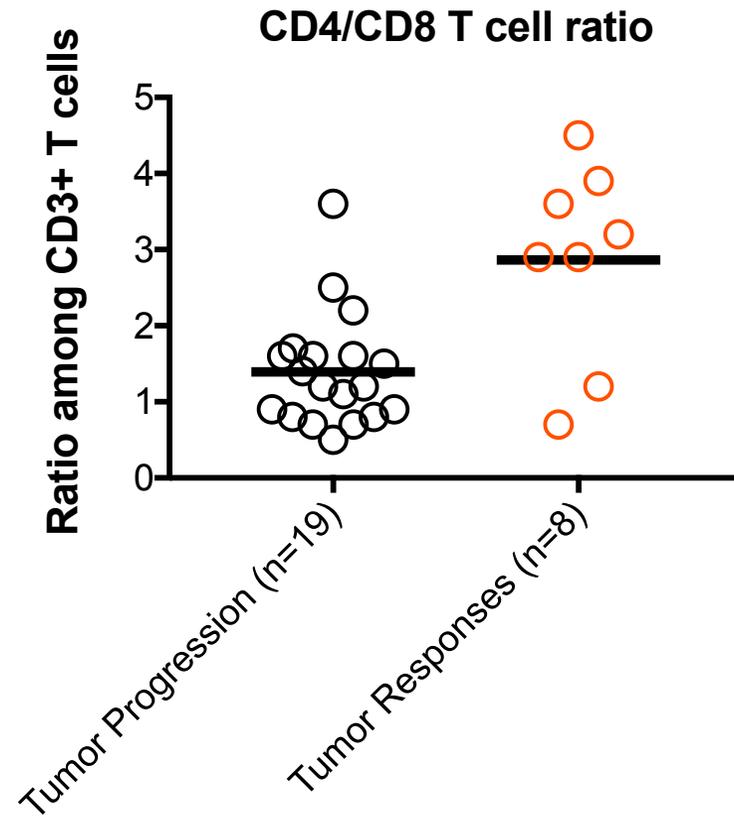
Normal CD4/CD8 ratio: median overall survival (mOS) = 409 days

Reduced CD4/CD8 ratio: mOS = 260 days



# Baseline CD4/CD8 Ratio is Not Associated with Those Patients Responding to VBI-1901 Treatment with AS01<sub>B</sub>

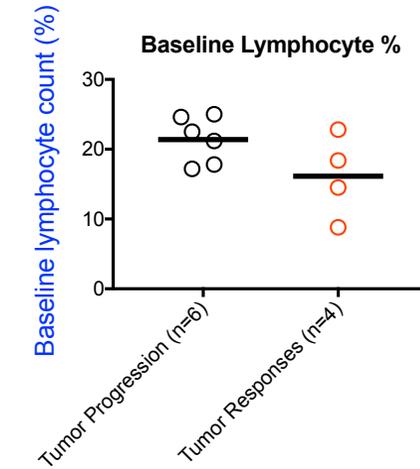
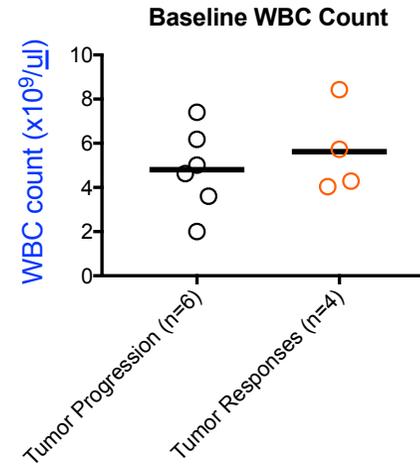
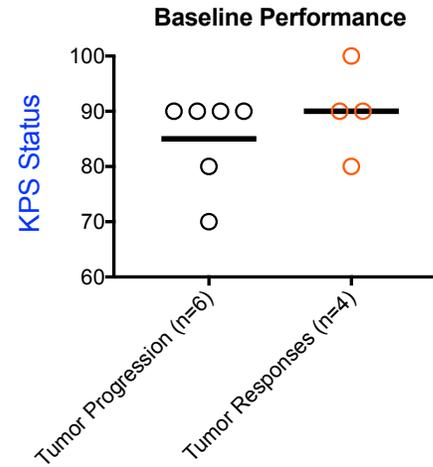
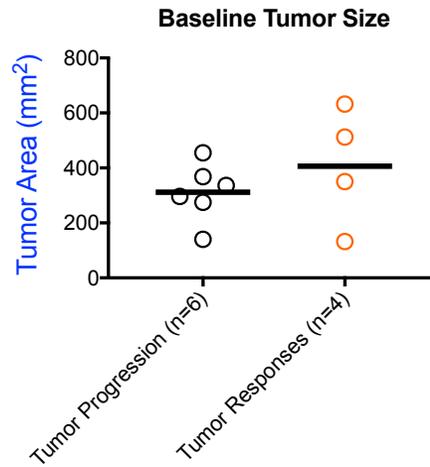
AS01 may help overcome deficits in immune fitness (low CD4/CD8 ratio)



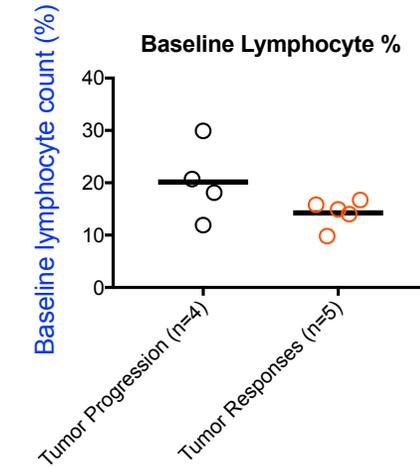
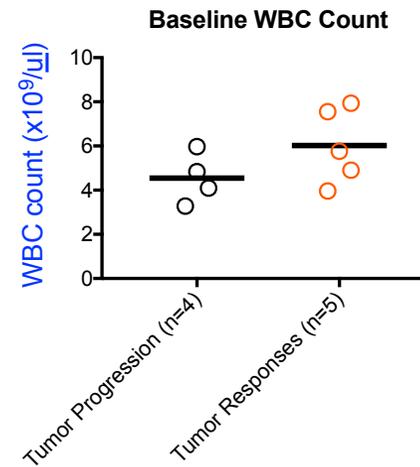
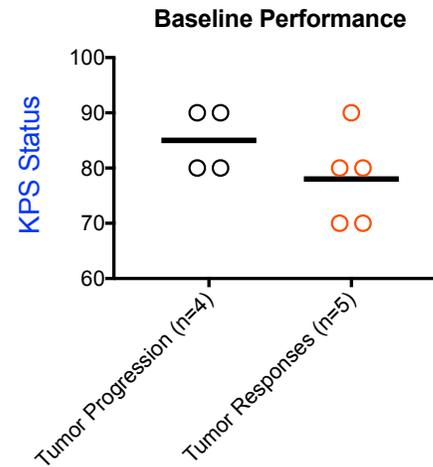
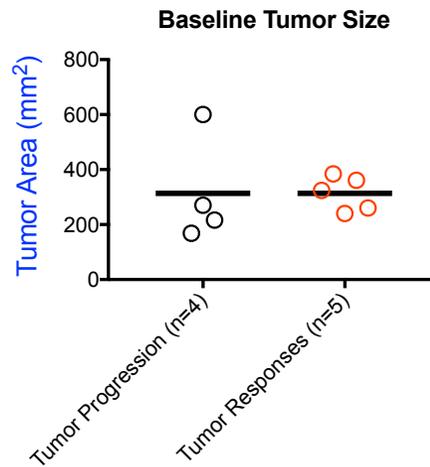
# Phase IIa (Part B) : Biomarker Data & Baseline Characteristics

Alternate Baseline Biomarkers are Not Associated with Those Patients Responding to VBI-1901 Treatment

GM-CSF arm



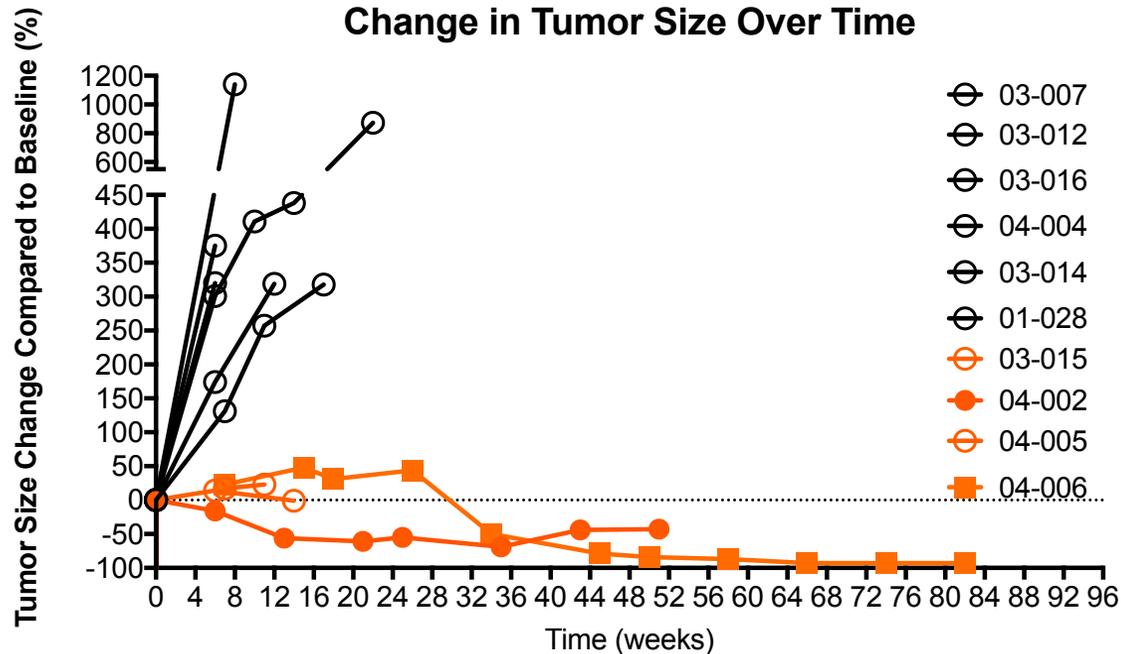
AS01<sub>B</sub> arm



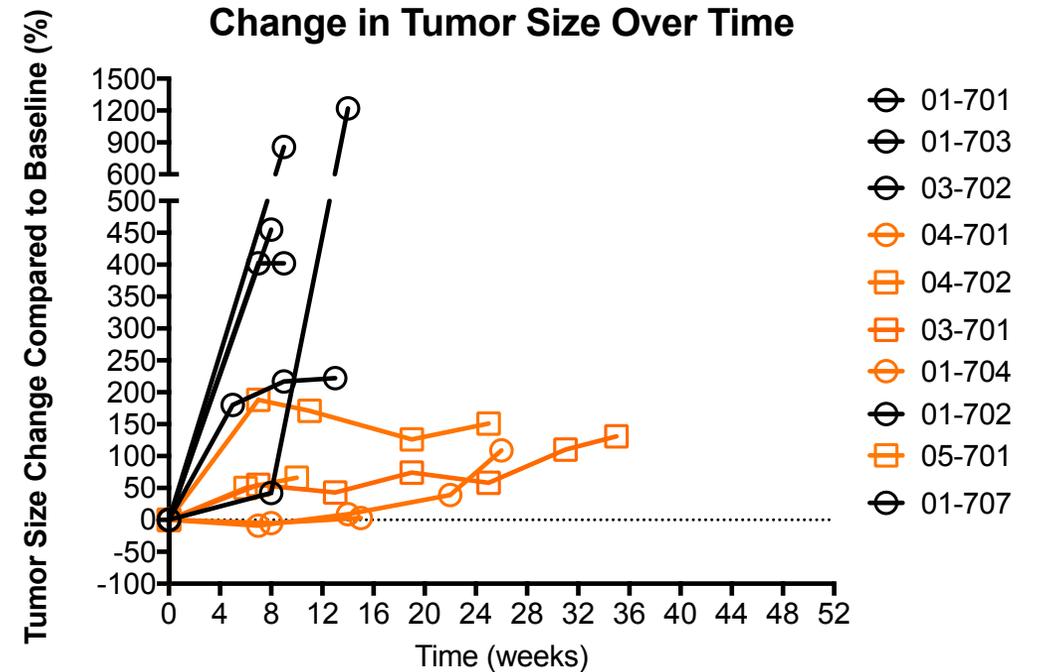
# Phase IIa (Part B) : Tumor Response Data

Disease Control Rates of 40% and 50% in GM-CSF and AS01B arms, respectively, in Part B of Trial

## VBI-1901 + GM-CSF



## VBI-1901 + AS01<sub>B</sub>

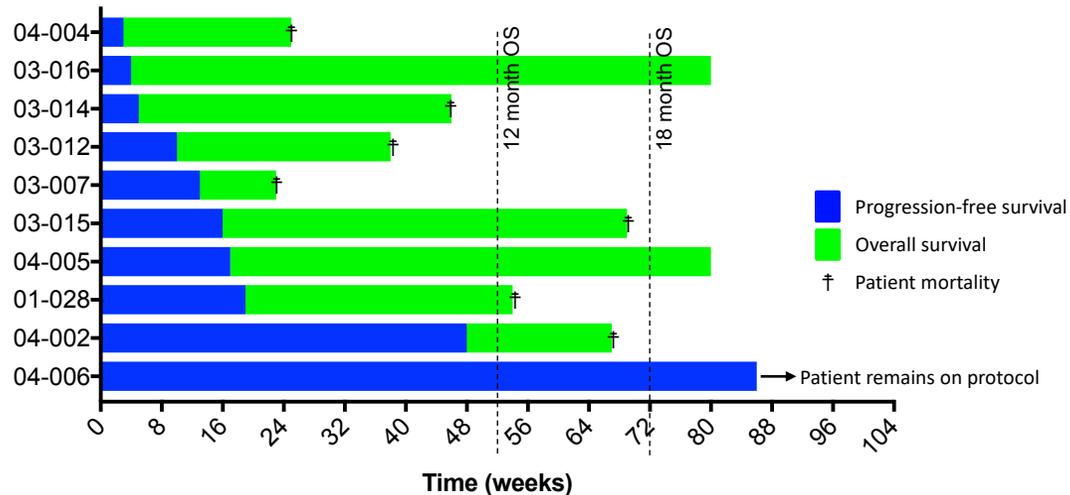


○ No tumor response    ○ Stable Disease    □ Pseudo Progression    ● Partial Response    ■ Partial Response with Pseudo Progression

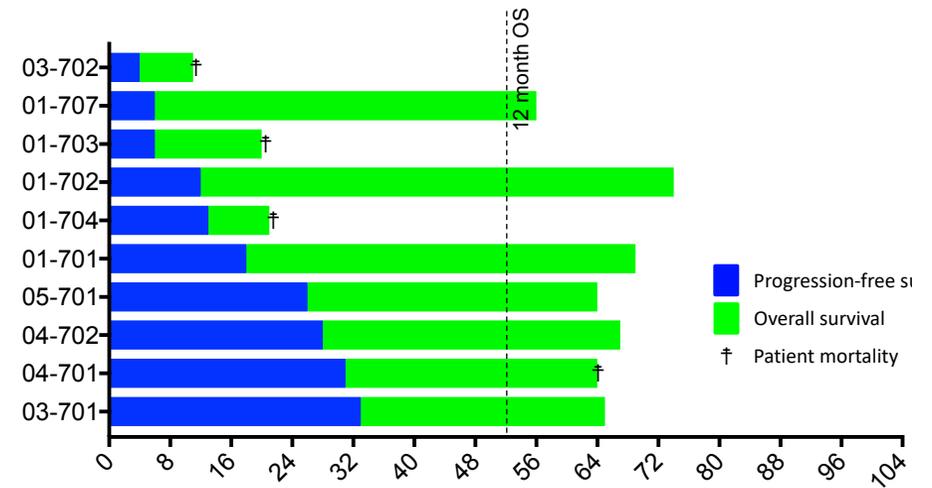
# Phase IIa (Part B) : Clinical outcomes

12-month Overall Survival (OS) rates of 60% and 70% compared to historical rate of ~30% (Taal *et al*, 2014)

VBI-1901 + GM-CSF



VBI-1901 + AS01<sub>B</sub>



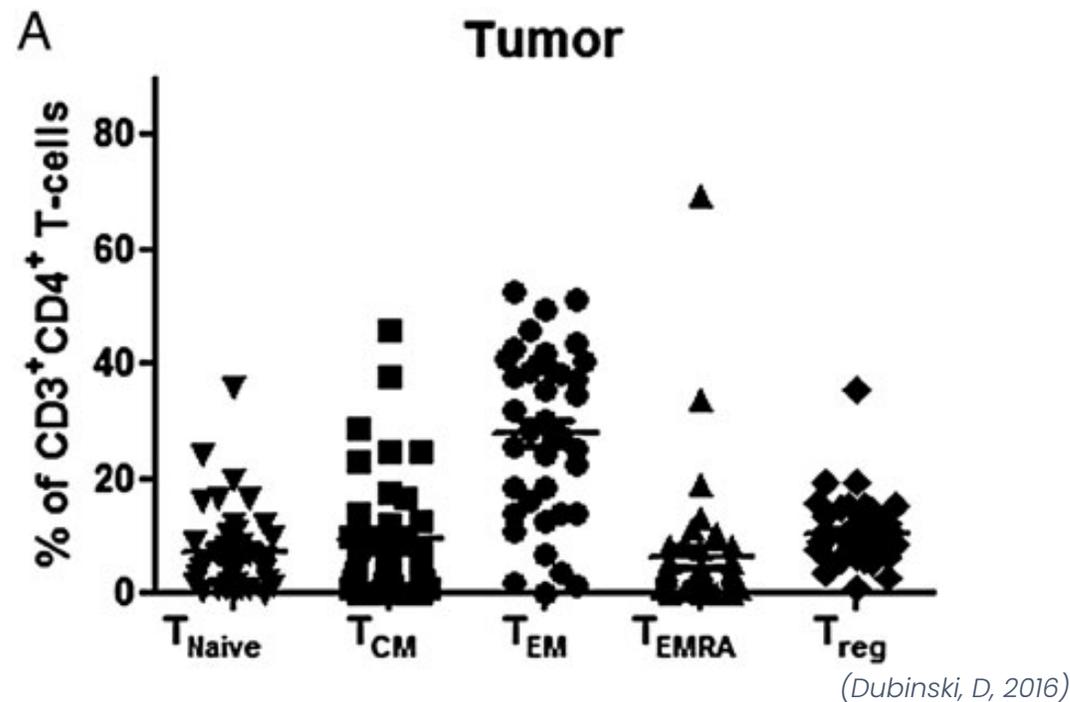
- Additionally, VBI-1901 + GM-CSF demonstrated 30% 18-month OS rate
- VBI-1901 + AS01<sub>B</sub> 18-month OS not yet reached



# How Do We Evaluate a Vaccine-Induced Tumor Response in the CNS by Measuring Responses in the Peripheral Blood?

CD4+ T cell responses are an often overlooked but critical component of productive tumor immunity

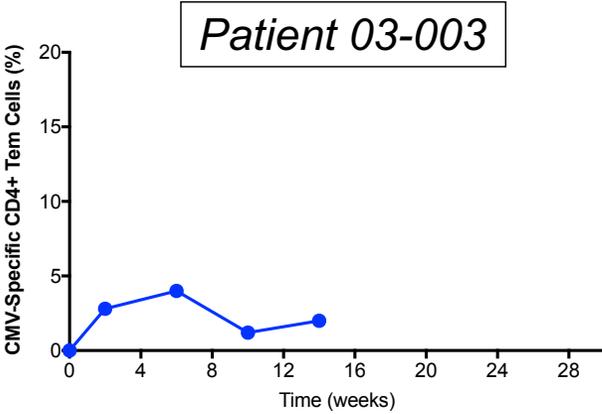
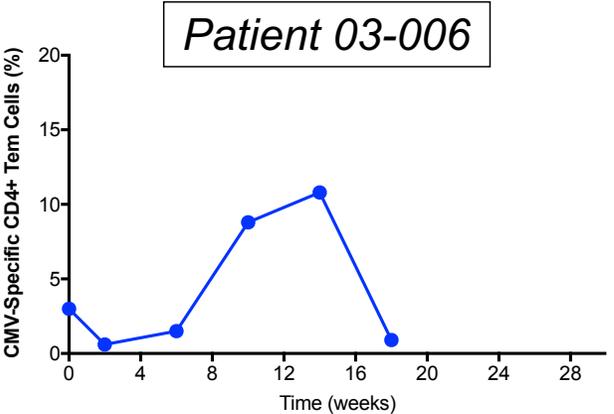
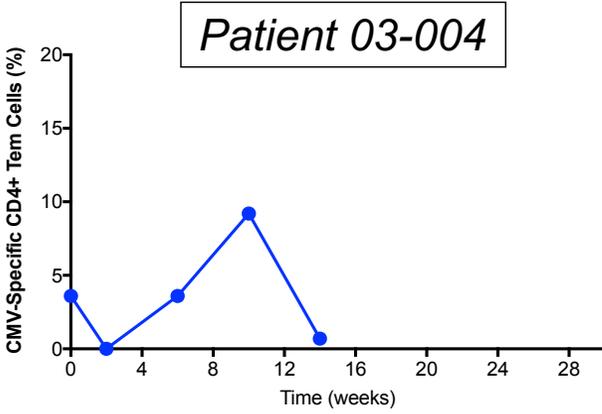
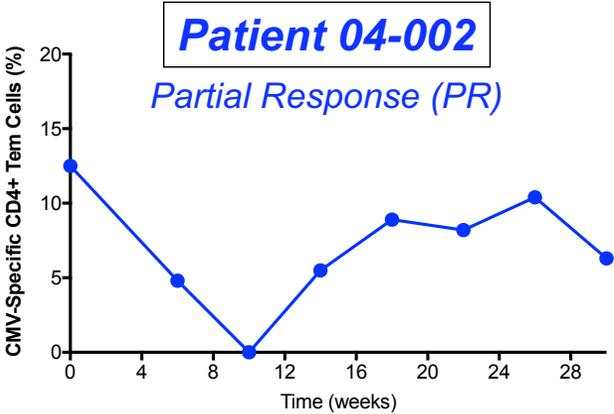
(Brightman SE (2020) *J Leukoc Biol* 107, 625–633; Borst J (2018) *Nat Rev Immunol* 18, 635–647)



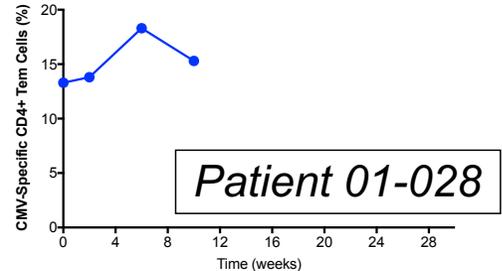
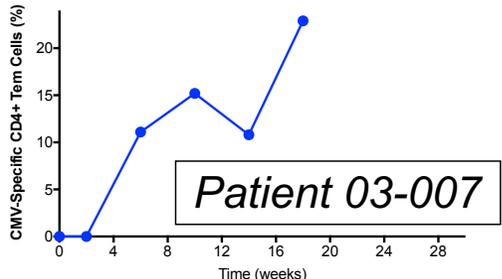
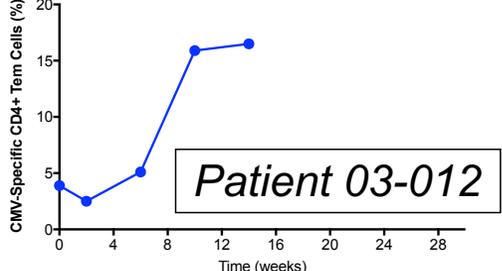
CD4+ effector memory cells are the dominant T-cell subset that infiltrates the GBM microenvironment

# Dynamic Loss/Boosting of CMV-Specific CD4+ Effector Memory Cells in Peripheral Blood of Tumor Responders in GM-CSF extension arm of Part B

## Tumor Responses



## Tumor Progression



# Summary of CMV-Specific GBM Immunotherapeutic Candidate, VBI-1901

VBI-1901 has demonstrated encouraging tumor responses in Phase I/IIa clinical study

- **VBI-1901 + GM-CSF** : Phase I/II Preliminary Conclusions

- VBI-1901+GM-CSF is safe and well tolerated
- 7/16 tumor responses in patients receiving high dose of VBI-1901 + GM-CSF (Parts A & B of the study)
  - Two subjects experienced a Partial Response (>50% reduction)
  - Two others experienced 50% reduction in primary tumor, but new lesions prevented I-RANO designation of Partial Response
- CD4/CD8 biomarker may identify those most likely to respond & derive benefit from VBI-1901 Tx

- **VBI-1901 + AS01<sub>B</sub>** : Phase I/II Preliminary Conclusions

- VBI-1901+AS01<sub>B</sub> is safe and well tolerated
- 5/10 tumor responses in patients receiving high dose of VBI-1901 + AS01<sub>B</sub>
  - Three experienced pseudo progression – strong indication of T-cell migration into tumor microenvironment
- AS01<sub>B</sub> avoids reliance on CD4/CD8 biomarker (potentially increasing number of patients who may benefit)

- **Next Steps**

- **Mid-Year 2022** : VBI expects to evaluate two cohorts of VBI-1901 in the INSIGhT trial, an on-going randomized, controlled, clinical study
- **Q1 2022** : VBI expects to initiate expansion of ongoing study in recurrent GBM, increasing study size and adding a control arm

