# Viracta Therapeutics, Inc. January 2024



### **Forward Looking Statements**

This communication contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995, which are based on current expectations, estimates and projections based on information currently available to management of Viracta Therapeutics, Inc. ("Viracta" or the "Company"), including, without limitation, statements regarding: Viracta's development pipeline; the details, timeline and expected progress for Viracta's ongoing trials; the expected ability of Viracta to undertake certain activities and accomplish certain goals with respect to its clinical program in EBV+ lymphoma, EBV+ solid tumors, other virus-associated malignancies or its programs; expectations regarding future therapeutic and commercial potential with respect to Viracta's clinical program in EBV+ lymphoma, EBV+ solid tumors or other virus-associated malignancies; the ability of Viracta to support multiple new drug application filings and approvals from the NAVAL-1 trial; Viracta's plans to meet with the FDA to discuss preliminary results from the NAVAL-1 trial, amending the NAVAL-1 protocol to add patients as necessary to enable registration and provide other program updates; the expected future milestones and key upcoming events and their significance; and other statements that are not historical facts. Risks and uncertainties related to Viracta that may cause actual results to differ materially from those expressed or implied in any forward-looking statement include, but are not limited to: Viracta's ability to successfully enroll patients in and complete its ongoing and planned clinical trials; Viracta's plans to develop and commercialize its product candidates, including all oral combinations of nanatinostat and valganciclovir; the timing of initiation of Viracta's planned clinical trials; the timing of the availability of data from Viracta's clinical trials; the possibility that previous preclinical and clinical results may not be predictive of future clinical results; the timing of any planned investigational new drug application or new drug application; Viracta's plans to research, develop and commercialize its current and future product candidates; the clinical utility, potential benefits and market acceptance of Viracta's product candidates; Viracta's ability to identify additional products or product candidates with significant commercial potential; developments and projections relating to Viracta's competitors and its industry; the impact of government laws and regulations; Viracta's ability to protect its intellectual property position; and Viracta's estimates regarding future expenses, capital requirements and need for additional financing.

These risks and uncertainties may be amplified by the COVID-19 pandemic, which has caused significant economic uncertainty. If any of these risks materialize or underlying assumptions prove incorrect, actual results could differ materially from the results implied by these forward-looking statements. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" and elsewhere in Viracta's most recent filings with the SEC and any subsequent reports on Form 10-K, Form 10-Q or Form 8-K filed with the SEC from time to time and available at <a href="https://www.sec.gov">www.sec.gov</a>. The forward-looking statements included in this communication are made only as of the date hereof. Viracta assumes no obligation and does not intend to update these forward-looking statements, except as required by law or applicable regulation.



### **Experienced Leadership Team**



Mark Rothera President and Chief Executive Officer



Daniel Chevallard, CPA Chief Operating Officer & Chief Financial Officer



Darrel P. Cohen, MD, PhD Chief Medical Officer

























Ayman Elguindy, PhD Chief Scientific Officer



Patric Nelson, MBA Senior VP, Business Dev. & Corporate











# A Clinical-Stage Precision Oncology Company Focused on the Treatment and Prevention of Virus-Associated Cancers that Impact Patients Worldwide



Adverse survival outcomes are seen with most Epstein-Barr virus (EBV)-associated cancers; need for targeted therapies *EBV-associated cancer incidence* >300,000 per annum (~2% of global cancer burden)



Nana-val, an all-oral combination approach targeting EBV<sup>+</sup> cancers with potential tumor agnostic MOA

Novel "Kick & Kill" Mechanism of Action



Pivotal NAVAL-1 study in multiple R/R EBV+ <u>lymphoma subtypes</u>; R/R EBV+ PTCL cohort enrolling patients in Stage 2

Speed to market strategy for lead R/R EBV+ PTCL cohort supported by accelerating pace of enrollment



Phase 1b/2 study in advanced EBV<sup>+</sup> solid tumors; evaluating new dosing regimen based on compelling preclinical data Enrollment underway into first split daily dosing cohort, plan to determine RP2D and initiate Phase 2 dose optimization cohort in 2024



Strategic path forward with multiple value-driving milestones

Anticipate complete enrollment of Stage 2 in the R/R EBV+ PTCL cohort in Q1 2024 and engagement with the FDA on potential accelerated approval pathway by mid-2024



## **Epstein-Barr Virus (EBV): A High Global Cancer Priority**

EBV+ malignancies account for ~2% of all new cancer cases globally

EBV positivity, by lymphoma subty	pe <sup>1, 2,3</sup>
Peripheral T-cell lymphoma* (PTCL)	40-65%
Diffuse large B-cell lymphoma (DLBCL)	5-15%
Post-transplant lymphoproliferative disorders (PTLD)	60-80%

EBV positivity, by solid tumor subtype <sup>4</sup>				
Nasopharyngeal carcinoma (NPC)	75-95%			
Gastric cancer (GC)	8-10%			

~90% of the adult population are infected with EBV

Latency confers resistance to antiviral therapies and facilitates evasion of immune detection >300,000 new cases/year of EBV+ lymphomas and solid tumors<sup>5</sup>

Responsible for ~180,000 cancer deaths/year<sup>5</sup>

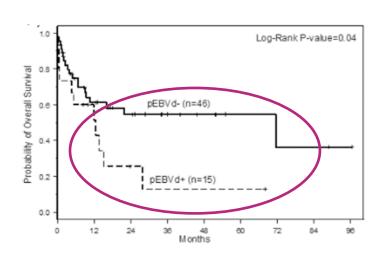
The incidence of EBV-associated cancers is likely greater, impacting more cancer types



# Viracta is Developing a Precision Medicine to Treat Unique Subsets of EBV+ Lymphoma with Adverse Survival Outcomes

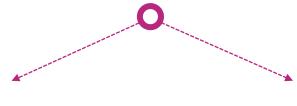
Currently limited or no targeted therapy options for EBV-associated cancers



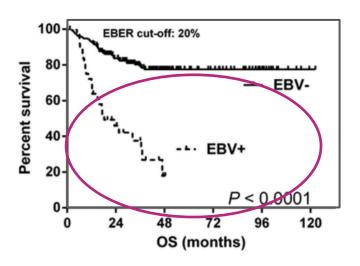


**PTCL EBV**+ Rate: 40-65%

Addressing patient populations with high unmet medical need



Diffuse Large B-cell Lymphoma<sup>2</sup> (Overall Survival)



DLBCL EBV+ Rate: 5-15%



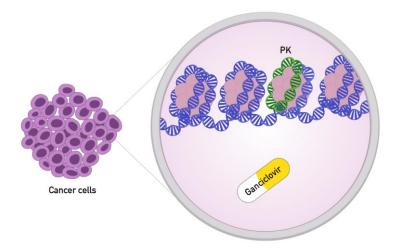
#### Nana-val: a Unique Approach to Targeting and Killing EBV+ Cancer Cells

Nanatinostat sensitizes EBV+ tumors to the cytotoxic effects of ganciclovir

#### **LATENCY**

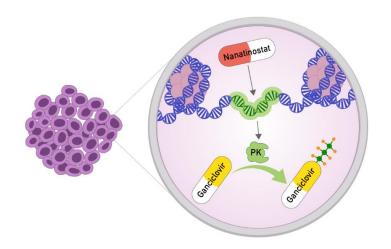
EBV is latent in cancer cells.

Valganciclovir, antiviral & cytotoxic prodrug of ganciclovir (GCV), is inactive in the absence of EBV protein kinase (PK)



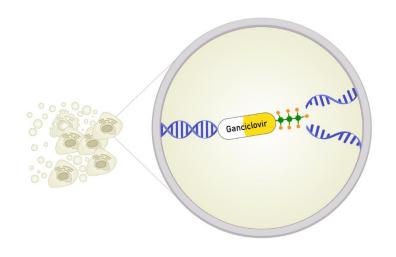
#### THE KICK

Nanatinostat potently induces expression of EBV protein kinase (PK), which activates GCV into its cytotoxic form



#### THE KILL

Activated GCV inhibits DNA replication leading to apoptosis of EBV+ cancer cells







Nana-val: R/R EBV+ Lymphoma Program

### NAVAL-1: Pivotal Phase 2 Trial in R/R EBV+ Lymphomas

Global study, with an adaptive Simon 2-stage design, focused on the largest EBV-positive lymphoma patient populations

#### **Patient population:**

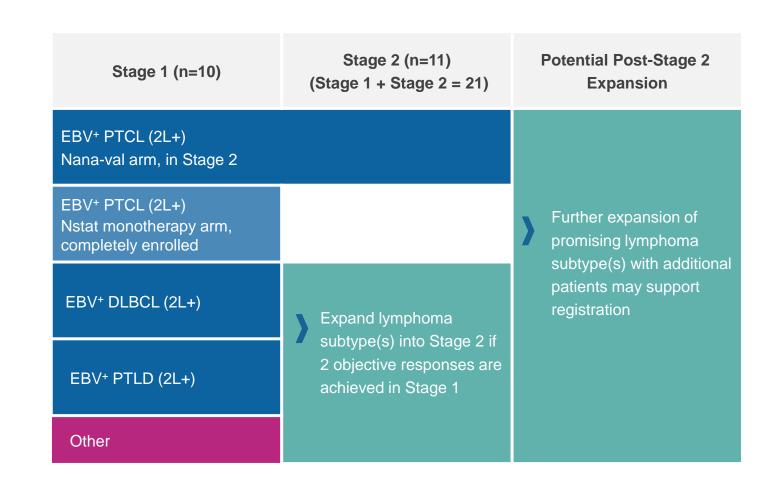
R/R EBV<sup>+</sup> lymphoma with ≥1 prior therapies and no curative options

Including pediatric EBV+ PTLD patients ≥12yrs

#### **Primary endpoint:**

- Objective response rate (ORR) by independent central review
- Potential to further expand indications with promising antitumor activity after Stage 2

Speed to Market strategy for lead R/R EBV<sup>+</sup>
PTCL cohort - anticipate complete enrollment
of Stage 2 in Q1 2024





# **Expanded and Extended Safety Data Demonstrated Nana-val Regimen was Generally Well-Tolerated**

# Treatment-Emergent Adverse Events Reported in >16 (>25%) Patients

	Study 201 (N=64)			
	Any	G4		
Thrombocytopenia	27 (42%)	8 (13%)	6 (10%)	
Neutropenia	25 (39%)	10 (16%)	11 (17%)	
Nausea	25 (39%)	2 (3%)	0	
Anemia	24 (38%)	12 (19%)	1 (2%)	
Fatigue	22 (34%)	4 (6%)	0	
Constipation	19 (30%)	1 (2%)	0	
Diarrhea	19 (30%)	1 (2%)	0	
Creatinine Increased	17 (27%)	1 (2%)	0	

#### Treatment-Emergent Serious Adverse Events Occurred in 23 of 64 (36%) Patients

Treatment-emergent serious adverse events occurring in more than 1 patient (n=2 each):

- febrile neutropenia
- atrial fibrillation
- sepsis
- pneumonia (pneumonia and viral pneumonia)
- dyspnea
- acute kidney injury
- Pyrexia

There were no study treatment-related deaths

Safety profile suggests potential for combining with other chemo- and/or immunotherapies





# R/R EBV+ PTCL:

T-cell lymphoma with high unmet medical need

### R/R EBV+ PTCL: Speed to Market Strategy for Nana-val

Completed enrollment of Stage 1 in Q4 2023; enrollment into Stage 2 continues to accelerate

- Completed enrollment of Stage 1 in Q4 2023
  - 2 cohort arms: patients treated with nanatinostat monotherapy (n=10) or with Nana-val (n=10)
- Anticipate reporting Stage 1 data at a medical meeting in H1 2024
- Anticipate complete enrollment of Stage 2 in Q1 2024
  - Nearly half of the 11 Stage 2 patients have been enrolled\*
- Plan to meet with FDA to discuss additional requirements for accelerated approval in mid-2024
- Enroll patients into the post-Phase 2 expansion cohort to support potential accelerated approval
- Anticipate presenting Stage 2 data in H2 2024



# PICL

# PTCL: Patient Journey and Treatment Options are Suboptimal\*

No established second-line treatment for PTCL

#### 1L Patients

#### **Combination Chemotherapy**

e.g. CHOP, CHOEP

CHP + CD30 antibody

# R/R PTCL Patients No Current SoC

#### Nana-val (2L Initial positioning)

#### **Salvage Chemotherapy**

Single agent

Combination regimen

#### **Other Agents**

**HDAC** inhibitors

CD30 antibody

**Clinical Trial** 

#### **Key Considerations**<sup>1</sup>

- PTCL is highly aggressive with limited treatment options
- 5-year event-free survival rate:
  - PTCL, NOS ~25% overall
  - EBV+ PTCL ~11%
- No current standard of care (SoC) for R/R PTCL
- For non-HCT candidates, chemotherapy is 1L, combination regimens preferred
- In R/R patients, single-agent chemotherapy is preferred to limit toxicity
- In R/R patients, other agents may be used guided by the subtype of PTCL and their toxicity profile

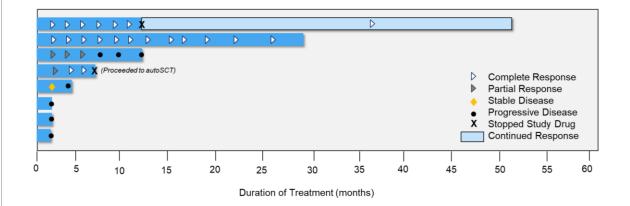




## R/R EBV+ PTCL: ORR and DoR Exceeds Current Approved Therapies

#### Initial data from the NAVAL-1 trial are consistent with Study 201 data

	Study 201 Data <sup>1</sup> (n=13)	NAVAL-1 (n=5*)
	Evaluable Patients <sup>2</sup> (n=8)	ITT (n=5)
Response		
ORR	4 (50%)	2 (40%)
CR	3 (38%)	2 (40%)
PR	1	0
SD	1	0
PD	3	2
Clinical Benefit Rate	5 (63%)	2 (40%)
Data Cutoff	May 4, 2023	June 30, 2023



- Median duration of response (DoR) for Study 201 is 17.3 months as of May 4, 2023
  - Median DoRs for other R/R PTCL therapies that have received AA were ~8.5-9.5 months
- Median DoR not yet reached in NAVAL-1 trial



#### Nana-val is Well Positioned for Potential Accelerated Approval in R/R EBV+ PTCL

Anticipate engagement with FDA in mid-2024 to align on accelerated registration pathway

Accelerated Approval Criteria	Nana-val: R/R EBV+ PTCL	
Unmet medical need population	No approved therapies for R/R EBV+ PTCL	<b>✓</b>
Rarity of the serious life-threatening disease without alternate available treatment options	EBV+ PTCL 5-year event-free survival rate of ~11%*	<b>✓</b>
Magnitude of the response rate observed	ORR of 30% - 45%+; CRR of ~25% - 40%	<b>✓</b>
Duration of response (DoR)	17.3 months median DoR observed in Phase 1b/2 study	<b>✓</b>
Favorability of the safety profile	Generally well-tolerated	<b>✓</b>

Base Case Assumption: ~60-90 total R/R EBV+ PTCL patients may be required in the NAVAL-1 trial for potential accelerated approval



# Nana-val Compared to Other Therapies that Received Accelerated Approval for the Treatment of R/R PTCL

Criteria	Nana-val*	Beleodaq** (Belinostat)	Istodax** (Romidepsin)	Folotyn** (Pralatrexate)
Indication(s)	R/R EBV+ PTCL	R/R PTCL (EBV+ & EBV-)	R/R PTCL (EBV+ & EBV-)	R/R PTCL (EBV+ & EBV-)
Overall Response Rate (ORR)	30-50%	25.8%	26.2%	26.6%
Complete Response Rate (CRR)	~25-40%	10.8%	15.4%	8.3%
Duration of Response (DoR)	17.3 months	8.4 months	<8.5 months	9.4 months
Sample Size	~60-90 (pending FDA confirmation)	120	130	109
Route of Administration	Oral	IV	IV	IV





#### EBV+ DLBCL Has a Significantly Worse Prognosis Compared to EBV- DLBCL

Recognized as a unique subtype of DLBCL with its own classification by the World Health Organization

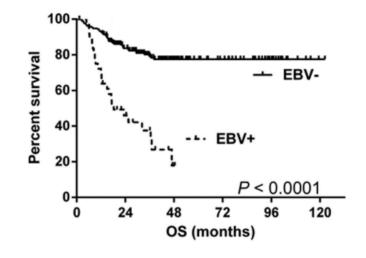
#### DLBCL is the most common lymphoma (~25% of all NHLs)

- ~5-15% of DLBCL cases are associated with EBV
- 5-year relative survival rate of ~64% overall
- Poor survival in R/R disease, current treatments offer modest response in 3L

#### EBV+ DLBCL is a clinically more aggressive subtype of DLBCL

- Survival rate is significantly less compared to EBV<sup>-</sup> disease
- Poor response/survival with standard immuno-chemotherapy
- Associated with distinct biologic features and mutational landscape
- Currently, no approved treatment options specifically targeting EBV+ DLBCL

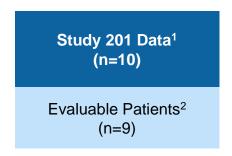
# Diffuse Large B-cell Lymphoma (Overall Survival)



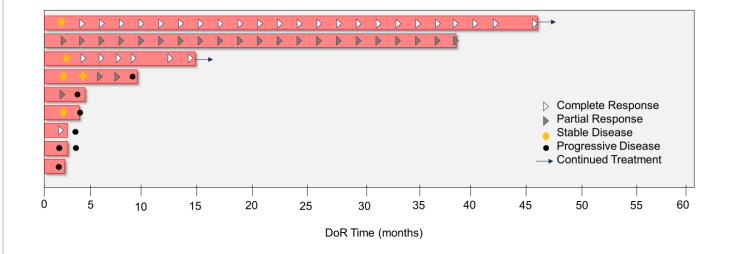


### R/R EBV+ DLBCL: Expanded Clinical Response Data

#### Early data suggests Nana-val delivers a compelling combination of ORR and DoR



Response	
ORR	6 (67%)
CR	3 (33%)
PR	3
SD	1
PD	2
Clinical Benefit Rate	7 (78%)
Data Cutoff	May 4, 2023



- Median Duration of Response (DoR) not yet reached
- 2 responding patients remain on study treatment with DoR times of ~11 months (CR) and ~42 months (CR) (as of May 2023)



# **Anticipated 2024 Milestones for NAVAL-1**

Trial	Indication	Q1:2024 Q2:2024		Q3:2024	Q4:2024
	R/R EBV+ PTCL	Q1:2024 - Complete enrollment of Stage 2 (n=11)		H2:2024 - Prese	ent Stage 2 data
	WK EBV FIGE		n both arms: nanatinostat with (n=10) or 10) valganciclovir		expansion cohort to support potential d approval
Nava-val Pivotal NAVAL-1 Trial	R/R EBV+ DLBCL				YE:2024 – Report Stage 1 data
(R/R EBV <sup>+</sup> Lymphomas)	R/R EBV+ PTLD				YE:2024 – Report Stage 1 data
	Regulatory Updates		Mid:2024 - Meet with the FDA to discuss additional requirements for accelerated approval		

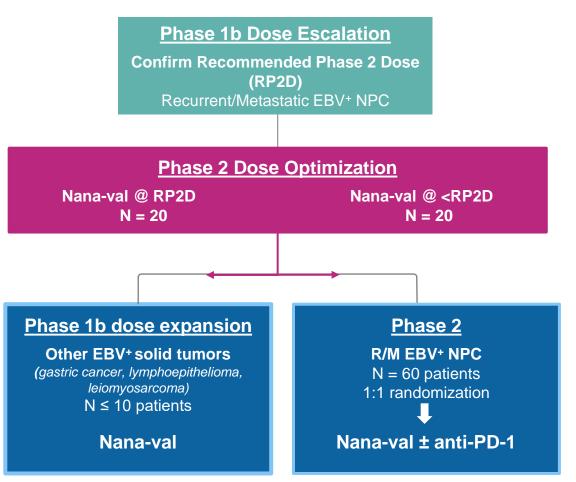




Nana-val: EBV+ Solid Tumor Program

## Nana-val Study "301": Phase 1b/2 Trial in Advanced EBV+ Solid Tumors

Open-label, multicenter study to evaluate the safety, tolerability, PK, and preliminary antitumor activity of Nana-val in patients with advanced EBV+ solid tumors



#### **Endpoints:**

- Primary:
  - Phase 1b: Incidence of dose-limiting toxicities
  - Phase 2: Objective response rate by RECIST v1.1
- Key Secondary:
  - Incidence and severity of AEs
  - Duration of response
  - Progression-free survival
  - Pharmacokinetic parameters

Anticipate initiating Phase 2 dose optimization cohort in 2024

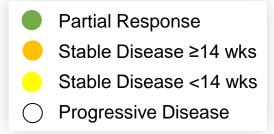


## Study 301: Responses to Date in Patients with R/M EBV+ NPC

Emerging evidence of dose response at higher doses and antitumor activity comparison of Dose Level 5 vs. Dose Level 2 suggest promise of split dosing approach

Dose Level	Nstat Oral Dose (Days 1-4/wk)	VGCV Oral Dose	N	Best Response
1	20 mg QD	900 mg QD	3	
2	30 mg QD	900 mg QD	4	0000
3	40 mg QD	900 mg QD	3	● ○ NE
4	10 mg split dose	900 mg BID x 21 d, then QD	3	00
5	20 mg / 10 mg split dose	900 mg BID x 21 d, then QD	4	

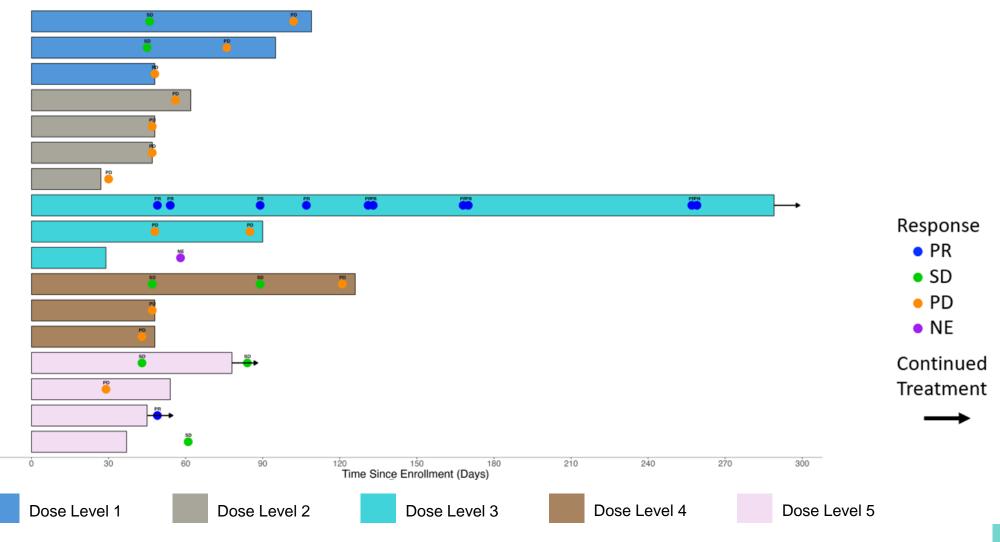
Partial responses confirmed at Dose Level 3 and Dose Level 5, both ongoing >10 months and >4 months on study treatment\*





### **Study 301: Swimmer Plot of Initial 5 Dose Cohorts**

2 confirmed PRs and 5 SDs within initial 17 patients (initial 5 dose cohorts)

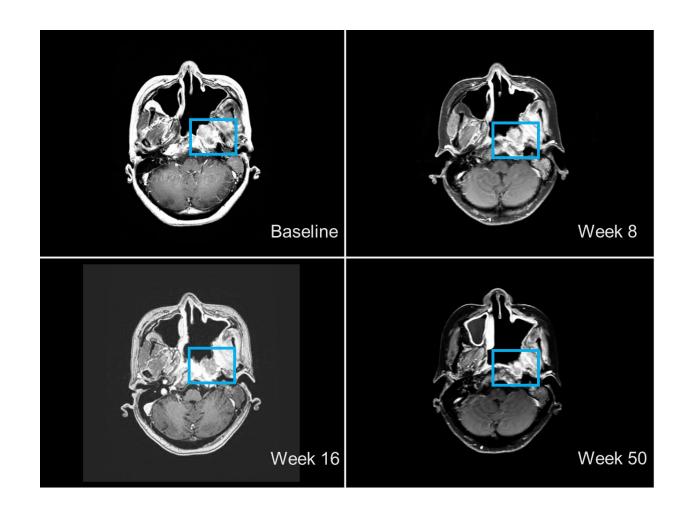




#### Study 301: MRI Scans of Confirmed Partial Response at Dose Level 3

#### >50% reduction in tumor size at 8-50 weeks

- 44-year-old female with locally recurrent EBV+ NPC (left nasopharynx)
- Disease previously progressed through chemoradiation therapy then combination chemotherapy
- Treated with nanatinostat 40 mg QD
   Days 1-4/week + VGCV 900 mg QD





### Nana-val has been Generally Well-Tolerated at Initial 5 Dose Levels

Preliminary safety data support continued dose escalation to determine RP2D

#### **Treatment-Related Adverse Events in ≥3 Patients**

Dose Level 1 = RP2D for R/R Lymphoma

		<b>Level 1</b> =3)		<b>Level 2</b> =4)		<b>Level 3</b> =3)		<b>Level 4</b> =3)		_ <b>evel 5</b> =4)
	G1-2	G3-4								
Nausea	1		2		2		1		1	
Decreased appetite	1		1		1		2		2	
Creatinine increased	1		2						2	
Fatigue	1		2			1	1			
Anemia	1		1							1
Lymphopenia			1				1	1		
Vomiting					2		1			

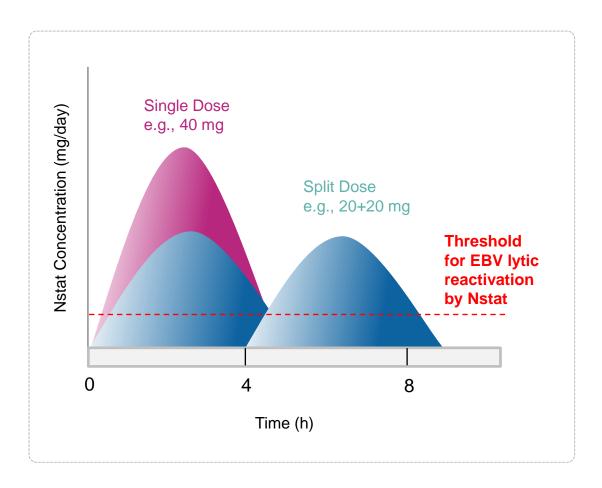
#### Safety

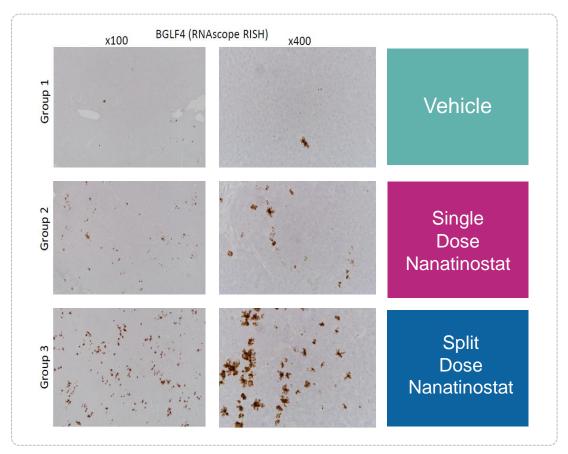
- No dose-limiting toxicities reported
- Majority of treatment-related adverse events were mild to moderate in severity



# Eight Hours Exposure to Nanatinostat Required for EBV Lytic Reactivation in Solid Tumors

Expression of EBV protein kinase (BGLF4) was markedly higher in animals treated with split dose Nstat

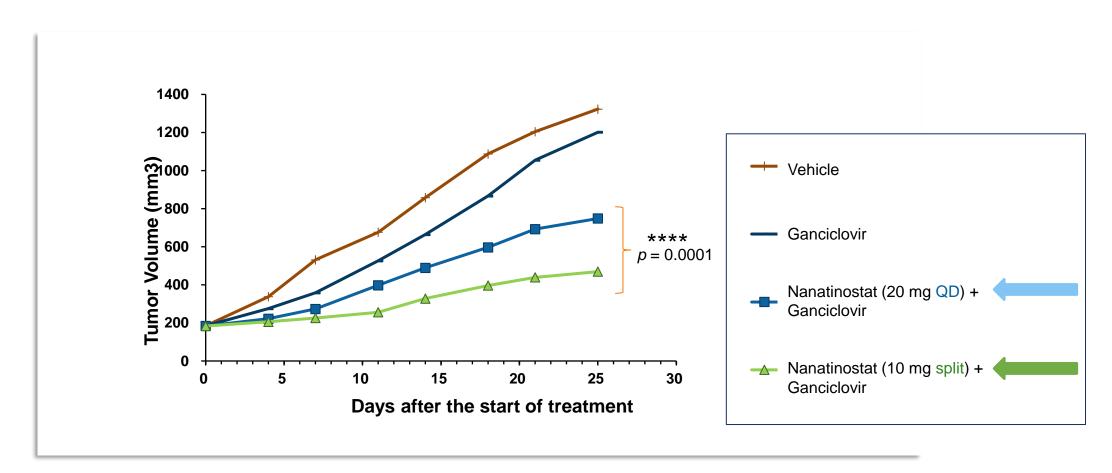






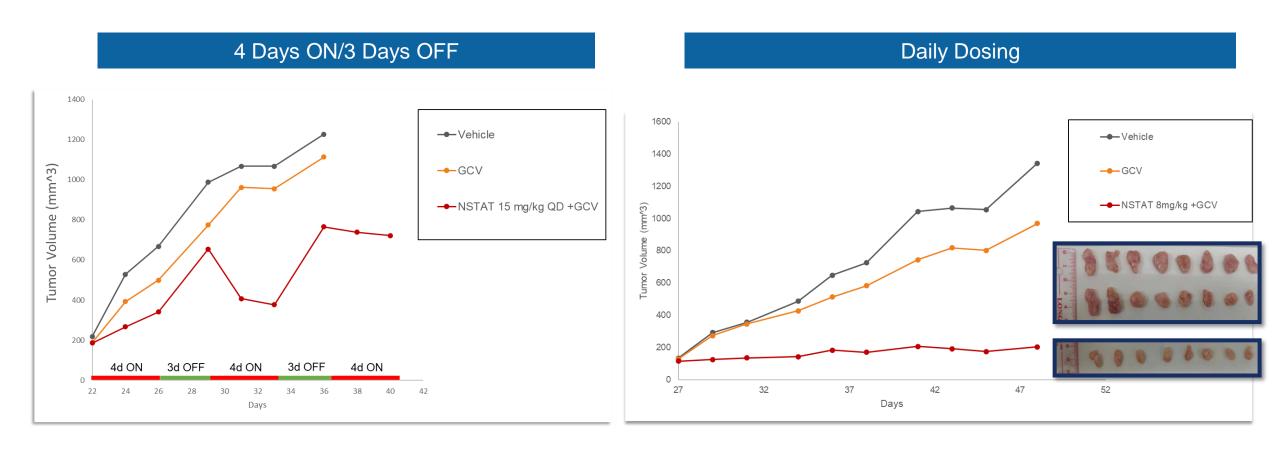
# Split Dosing Augments the Anti-Tumor Activity of Nana-val in Xenograft Model

Anti-tumor activity of SNU-719 subcutaneous xenograft model in B-NDG mice





# Dosing Schedule of 4 Days ON/3 Days OFF Allows Solid Tumor Regrowth, but Daily Dosing Renders Potent Anti-Tumor Activity in Xenograft Model





# Rationale for Split Daily Dosing (SDD) of Nanatinostat in Combination with Valganciclovir

Compelling preclinical data provides supporting evidence to evaluate a new dosing regimen



**Split dose** (2-4 hours apart) increases expression of EBV protein kinase, BGLF4



**Split dose** Significantly increased the anti-tumor activity of Nana-val in murine EBV<sup>+</sup> gastric cancer xenograft model



**Daily dosing** Enables increased anti-tumor activity relative to 4 days on 3 days off



**Higher doses** Safety data suggest patients with NPC can withstand higher doses of nanatinostat compared to lymphoma patients

SDD of Nanatinostat offers a potential to extend Nana-val patent portfolio with differentiated strategy from lymphoma; US provisional application(s) have been filed

Enrolling first cohort utilizing novel Split Daily Dosing (SDD) regimen to determine RP2D, up to 3 dose levels planned



#### Additional Dose Levels Planned on an SDD Schedule to Select RP2D

**Enrollment into Dose Level 6 anticipated before year-end 2023** 

Dose Level	Nstat Oral Dose	VGCV Oral Dose	N	Best Response
1	20 mg QD (4 days/wk)	900 mg QD	3	
2	30 mg QD (4 days/wk)	900 mg QD	4	0000
3	40 mg QD (4 days/wk)	900 mg QD	3	● ○ NE
4	10 mg split dose (4 days/wk)	900 mg BID x 21 d, then QD	3	
5	20 mg / 10 mg split dose (4 days/wk)	900 mg BID x 21 d, then QD	4	
<b>)</b> 6	20 mg / 20 mg SDD	450 mg / 450 mg SDD		
7	30 mg / 30 mg SDD	450 mg / 450 mg SDD		
8	40 mg / 40 mg SDD	450 mg / 450 mg SDD		Partial Response
				Stable Disease ≥14 v Stable Disease <14 v  ○ Progressive Disease

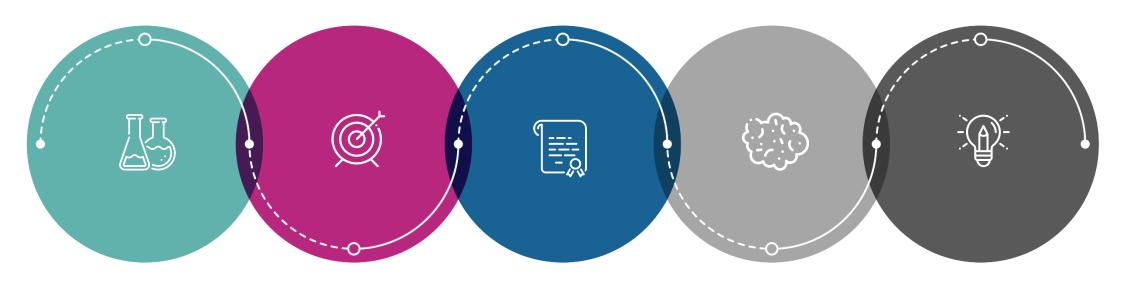


# **Anticipated 2024 Milestones for Nana-val**

Trial	Indication	Q1:2024	Q2:2024	Q3:2024	Q4:2024
	R/R EBV+ PTCL	Q1:2024 - Complete enrollment of Stage 2 (n=11)  H1:2024 - Report Stage 1 data from without (n=10)	both arms: nanatinostat with (n=10) or ) valganciclovir	Enroll patients into the post-Phase 2	ent Stage 2 data expansion cohort to support potential approval
Nava-val Pivotal NAVAL-1 Trial	R/R EBV+ DLBCL				YE:2024 – Report Stage 1 data
(R/R EBV <sup>+</sup> Lymphomas)	R/R EBV+ PTLD				YE:2024 – Report Stage 1 data
	Regulatory Updates		Mid:2024 - Meet with the FDA to discuss additional requirements for accelerated approval		
Nana-val Phase 1b/2 Study 301	NPC				ng the novel split daily dosing regimen at vels of Nana-val
(Advanced EBV+ Solid Tumors)					YE:2024 - Initiate Phase 2 dose- optimization cohort to confirm RP2D



# Focus is Maximizing the Nana-val Opportunity



Adverse survival outcomes are seen with many EBV-associated cancers

Need for targeted therapies

Well-tolerated, all-oral combination approach to targeting EBV+ cancers

Potential tumor agnostic
MOA; strengthened clinical
data

Pivotal NAVAL-1 trial in multiple R/R EBV<sup>+</sup> lymphoma subtypes

Completion of Stage 2 enrollment in PTCL cohort and engagement with FDA anticipated in mid-2024 Phase 1b/2 study in advanced EBV<sup>+</sup> solid tumors

Plan to determine RP2D and initiate Phase 2 dose-optimization in 2024 Lean operating model and a <u>speed to market</u> strategy

Regulatory validation with orphan drug designation granted for Nana-Val (across six indications)



# Thank you





## **US Incidence Estimates for EBV+ Hematological Malignancies**



Incidence and % EBV Positivity by Lymphoma Subtype					
Subtype	Annual (newly diagnosed)	R/R	Total	EBV Positivity	
Peripheral T-cell lymphoma (PTCL)*	~2,600	~1,100	~3,600	40%-65%	
Diffuse large B-cell lymphoma (DLBCL)	~27,700	~13,800	~41,500	5%-15%	
PTLD	~1,300	~700	~2,000	60%-80%	

The diagnosed incidence of EBV-associated hematological malignancies is likely underestimated given inconsistent testing due to the absence of an actionable targeted and actionable therapy



# Global Incidence Estimates for Priority EBV+ Hematological Malignancies

Nana-val has the potential to address other EBV<sup>+</sup> hematological malignancies

Incidence and % EBV Positivity by Lymphoma Subtype						
Subtype	Annual (newly diagnosed)	R/R	Total	EBV Positivity		
Peripheral T-cell lymphoma (PTCL)*	~15,200	~6,300	~21,500	40%-65%		
Diffuse large B-cell lymphoma (DLBCL)	~113,000	~56,000	~169,000	5%-15%		
PTLD	~9,100	~4,600	~13,700	60%-80%		

The diagnosed incidence of EBV-associated hematological malignancies is likely underestimated given inconsistent testing due to the absence of an actionable targeted and actionable therapy

