Viracta Therapeutics, Inc.

Business Update – August 14, 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 www.sec.gov. 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.





Introduction:

Mark Rothera

President and Chief Executive Officer



Expert Key Opinion Leader on Today's Call: Pierluigi Porcu, M.D.



Professor of Medical Oncology, Director of the Division of Hematologic Malignancies and Hematopoietic Stem Cell Transplantation, Department of Medical Oncology at Thomas Jefferson University



Today's Presenters from Viracta





Darrel P. Cohen, MD, PhD

Chief Medical Officer

Mike Faerm

Chief Financial Officer



Today's Agenda

Vision of Nana-val in EBV+ Cancers	Mark Rothera, President and Chief Executive Officer
Unmet Medical Need in EBV+ PTCL	Pierluigi Porcu, MD , Thomas Jefferson University
NAVAL-1 Trial Combined Stages 1 and 2 PTCL Data and Updated Clinical/Regulatory Plans	Darrel P. Cohen, MD, PhD, Chief Medical Officer
Anticipated Milestones	Mike Faerm, Chief Financial Officer
Closing Remarks	Mark Rothera , President and Chief Executive Officer
Q&A	

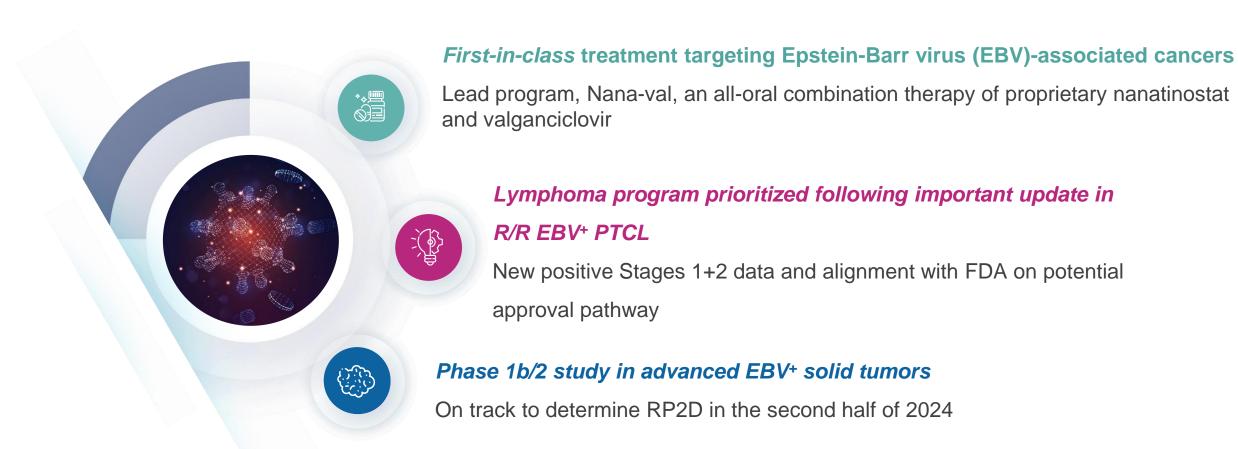




Vision of Nana-val in EBV+ Cancers

Mark Rothera, Viracta CEO

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





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

EBV+ malignancies account for ~2% or >300,000 of all new lymphoma and solid tumor cases globally

EBV positivity, by lymphoma subtype ^{1, 2,3}		
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 ⁴		
Nasopharyngeal carcinoma (NPC)	75-95%	
Gastric cancer (GC)	8-10%	

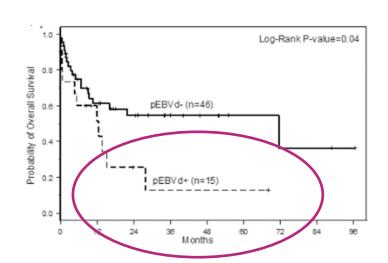
Actual number of EBV-positive cases likely underreported due to inconsistent EBV testing in the absence of an actionable EBV-targeted therapy



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

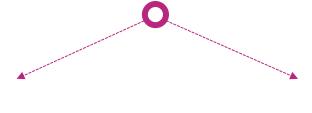
Currently limited or no targeted therapy options for EBV-associated cancers

Peripheral T-cell Lymphoma¹ (Overall Survival)

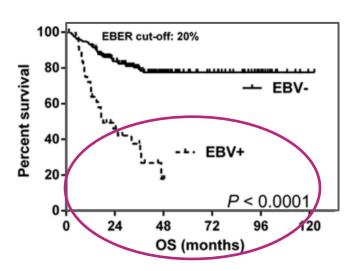


PTCL EBV+ Rate: 40-65%

Addressing patient populations with high unmet medical need



Diffuse Large B-cell Lymphoma² (Overall Survival)



DLBCL EBV+ Rate: 5-15%



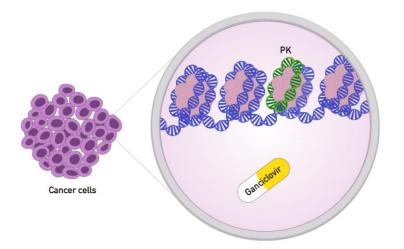
Nana-val: a Unique Approach to Targeting and Killing EBV+ Cancer Cells

Nanatinostat sensitizes EBV+ tumors to the cytotoxic effects of ganciclovir

LATENCY

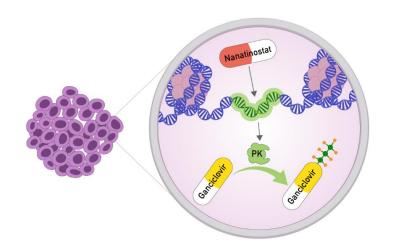
EBV is latent in cancer cells.

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



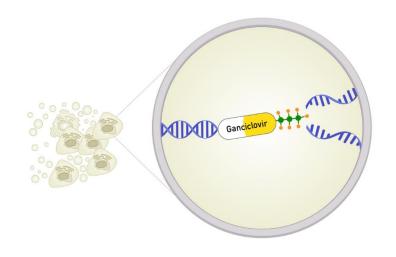
THE KICK

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







Unmet Medical Need in EBV+ PTCL

Pierluigi Porcu, M.D.

Approximately 70% of Patients Develop Relapsed or Refractory Disease After Frontline PTCL Therapy



Therapeutic challenges in peripheral T-cell lymphoma

Yunpeng Luan [™], Xiang Li, Yunqi Luan, Junyu Luo, Qinzuo Dong, Shili Ye, Yuejin Li, Yanmei Li, Lu Jia, Jun Yang & Dong-Hua Yang [™]

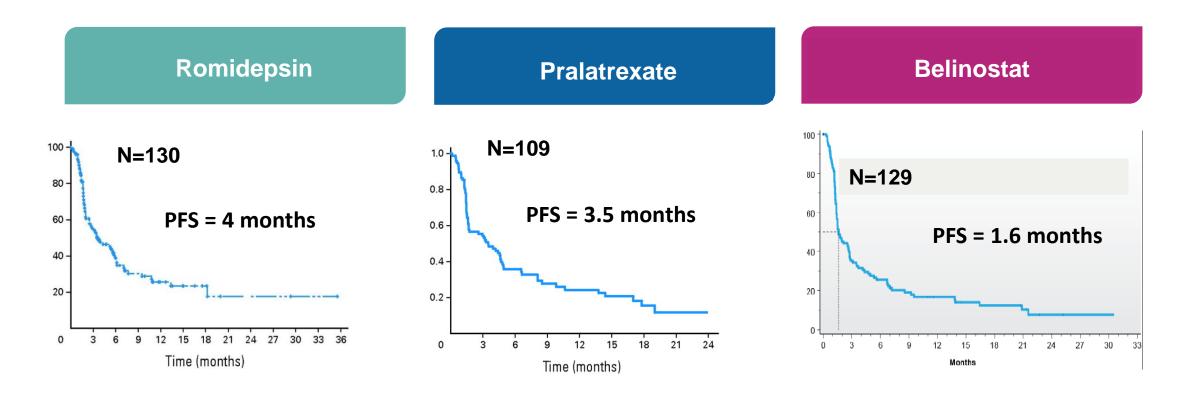
Molecular Cancer 23, Article number: 2 (2024) | Cite this article

3314 Accesses | **3** Citations | Metrics

- Despite availability of various treatment options, none have been universally curative, and eventually, drug resistance may develop in response to available treatments
- Multiple mechanisms, such as tumor heterogeneity, tumor microenvironment and signaling pathways, contribute to PTCL resistance
- Most PTCL subtypes are aggressive and chemotherapy-resistant, and their prognosis remains poor



Poor Prognosis for Patients with R/R PTCL



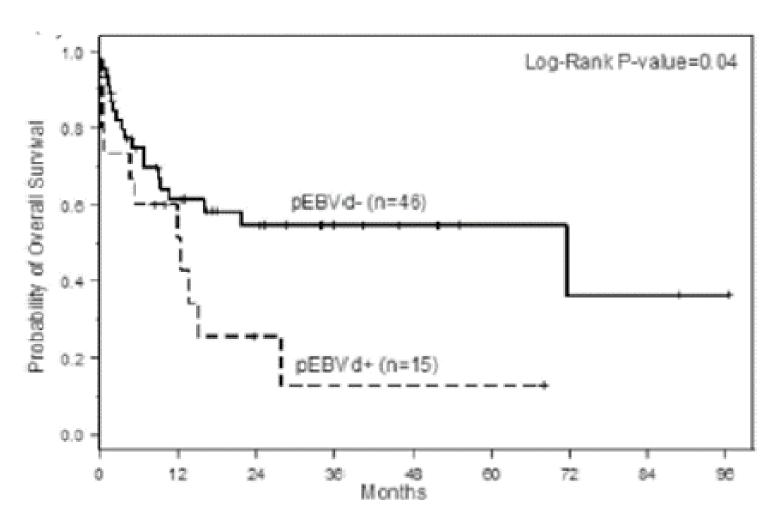
Mak V et al. JCO 2013;31:1970-1976; O'Connor OA, et al. *J Clin Oncol.* 2011;29:1182-1189; Coiffier B, et al. *J Clin Oncol.* 2012; 30:631-636; O'Connor OA et al ASCO 2013; Pro B, et al. J Clin Oncol. 2012;30:2190-2196; Horwitz S M et al. Blood 2014; 123:3095-3100

Modified from Horwitz S.



EBV Positivity Further Exacerbates Already Poor PTCL Survival Outcomes

Similarly, EBV+ PTCL may have worse available treatment outcomes than those with EBV- PTCL



EBV-positive PTCL is a **more aggressive disease** with a much poorer prognosis than EBV-negative PTCL.

EBV infection:

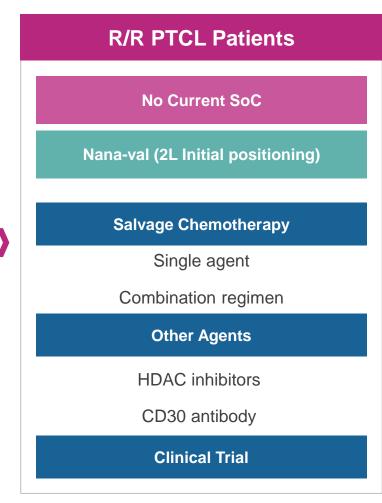
- contributes to oncogenesis
- inhibits apoptosis
- downregulates the innate immune response
- activates cell proliferation, angiogenesis, and metastasis.



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



Key Considerations¹

- 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



Case Study: EBV+ PTCL, subtype Angioimmunoblastic T-cell Lymphoma (AITL)

53 year old AAF, no PMH

Box A

Diffuse LAD (max 2.3 cm), B symptoms, TLS

- Cervical LN excisional biopsy: AITL
- IHC: CD3⁺, CD4⁺, CD5⁺, CD10⁺, BCL-6⁺, CD30⁺
- EBER-ISH positive (HIV-, HBV-, HCV-)
- BM Biopsy: negative
- CT C/A/P: Diffuse adenopathy; Stage III, IPI 2
- EBV DNA PCR not done (outside hospital)

Post-3L Therapy Progression

Box C

Box D

- Declining PS, G4 pancytopenia, AKI
- CTAP: New splenomegaly (18 cm)
- LDH: >1,000 IU/mL
- Repeat biopsy: AITL
- IHC: CD3+, CD4+, CD5+, CD10+, BCL-6+, CD30^{NEG}
 - EBER-ISH Positive
- BM biopsy positive (25%)

1L Therapy

Box B

- EPOCH x 1 (inpatient) > 5 cycles of BV-CHP
- EOT PET: Complete Metabolic Response (CMR)
- Auto SCT consolidation
- Nodal Progression 10 months later

2L Therapy

- Romidepsin x 4 cycles (months)
- PET2: Stable Disease; PET4 Disease Progression
- Hypercalcemia, AKI, elevated LFTs, ECOG=2

3L Therapy

- Gem/Ox x 1 cycle > septic shock

Subsequent Course

- Steroids (Dex) for anemia and CRS
- Continuous decline of PS
- Persistent pancytopenia, elevated LFTs, Ferritin
- Diagnosis of HLH-like syndrome
- Admitted > Transitioned to hospice care

EBV viral load (c/mL)

- May: 5,147

- June: 11,798

- July: 61,982

Ferritin (ng/ml)

- May: 501

- June: 2,187

- July: 10,820

sIL-2R (pg/ml)

- May: 26,000

- June: 18,200

- July: 53,000



NAVAL-1 Trial Stages 1+2 PTCL
Data and
Updated Clinical/Regulatory Plans
Darrel Cohen, Viracta CMO

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:

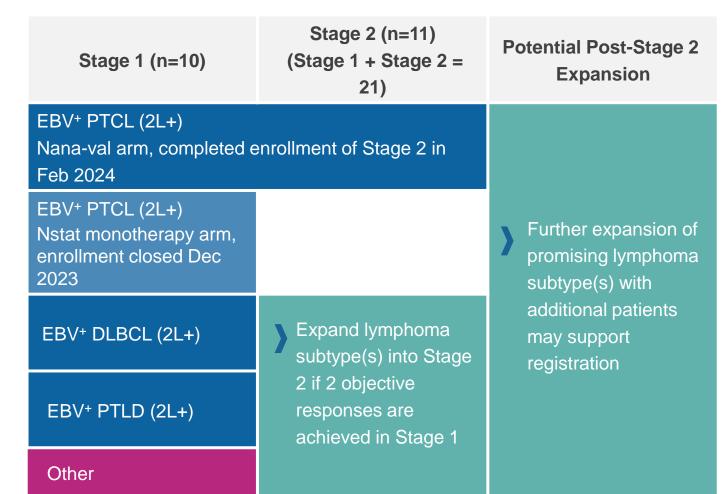
- R/R EBV+ lymphoma with ≥1 prior therapies and no curative options
 - Including pediatric EBV+ PTLD patients ≥12 yrs

PTCL cohort randomization:

 Patients randomized to either Nana-val or Nstat monotherapy in Stage 1

Primary endpoint:

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









Characteristic	Patients Enrolled in Nana-val Combination Stages 1 and 2 (N = 21)
Median age (y), [range]	69.0 [47-85]
Male / Female	13 / 8
ECOG performance status, Unknown / 0 / 1 / 2	4/15/2
 Ethnicity WHITE ASIAN BLACK OR AFRICAN AMERICAN NOT REPORTED / UNKNOWN 	13 (61.9%) 4 (19.0%) 2 (9.5%) 2 (9.5%)
PTCL subtype • AITL • PTCL-NOS	17 (81.0%) 4 (19.0%)
Prior lines of therapy	10 (47.6%) 8 (38.1%) 3 (14.3%)
Median number of prior therapies [range]	2 [1-4]
Stage • Unknown • I-II • III-IV	2 (9.5%) 4 (19.0%) 15 (71.4%)



All-Oral Regimen of Nana-val was Generally Well-Tolerated



Consistent with the known safety profile from over 150 patients treated with Nana-val

Most Frequently Occurring (≥10%) Treatment-Related Treatment-Emergent Adverse Events by Severity Grade and Preferred Term

Preferred Term ^[1]	Stages 1 and 2 Nana-val (N=21)		
	AII ^[2]	Grade 3/4	
Fatigue	4 (19.0%)	0	
Nausea	4 (19.0%)	0	
Decreased appetite	3 (14.3%)	0	
Diarrhoea	3 (14.3%)	1 (4.8%)	
Platelet count decreased	3 (14.3%)	1 (4.8%)	

¹Adverse events were coded to preferred terms using MedDRA, version 26.0



²One patient had Grade 5 pancytopenia and sepsis





Nana-val R/R EBV+ PTCL Stages 1 and Stage 2 Responses by Analysis Population

Analysis Population	ORR	CRR	CBR*
Intent-to-Treat ¹	7/21 (33%)	4/21 (19%)	10/21 (48%)
Efficacy-Evaluable ^{1,2}	7/17 (41%)	4/17 (24%)	10/17 (59%)
2L Intent-to-Treat ¹	6/10 (60%)	3/10 (30%)	8/10 (80%)
2L Efficacy-Evaluable ^{1,2}	6/9 (67%)	3/9 (33%)	8/9 (89%)

^{*}Includes 2 SDs in patients with 2L PTCL at Week 16 and 1 SD in patient with 3L PTCL at Week 16

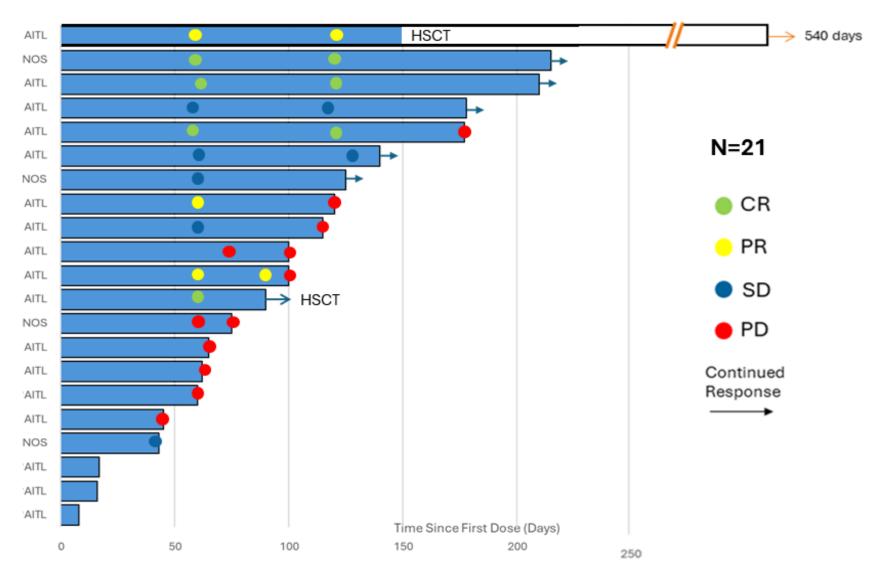


¹Investigator assessed; ²Eligible patients who have at least 1 post-baseline radiographic assessment

Nana-val 2L+ EBV+ PTCL Patient Responses (Stages 1 and 2)



Median Duration of Response not yet reached with 7 patients still on study treatment or post-HSCT

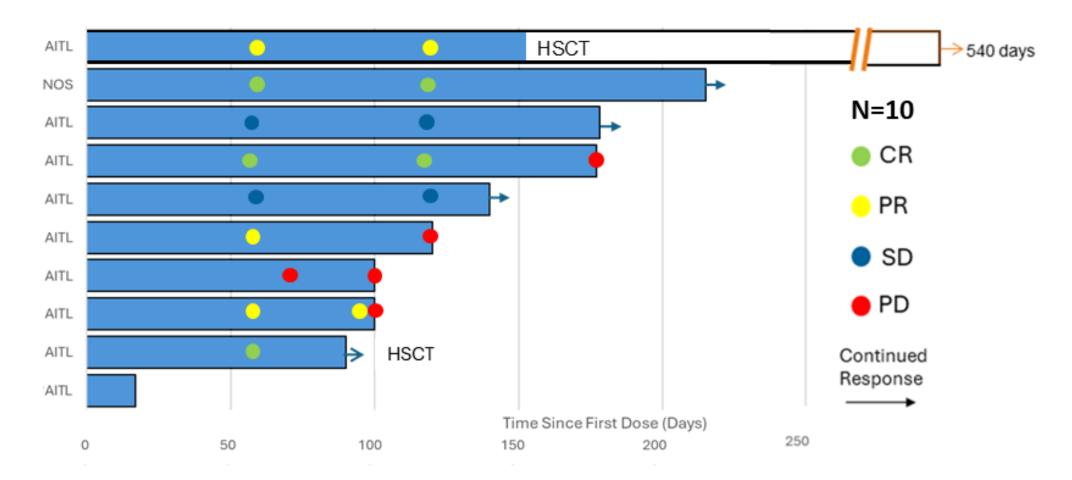




Nana-val <u>2L</u> EBV⁺ PTCL Patient Responses (Stages 1 and 2)



Median Duration of Response not yet reached with 5 patients still on study treatment or post-HSCT

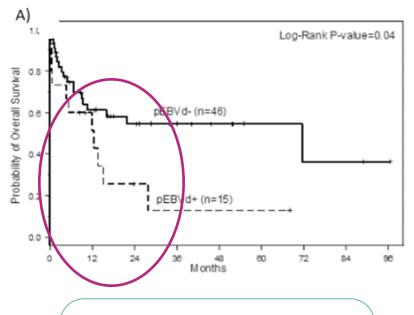




EBV+ PTCL Patients Progress <u>Very</u> Rapidly, and thus Treating Early with an EBV-Targeted Treatment Is Essential

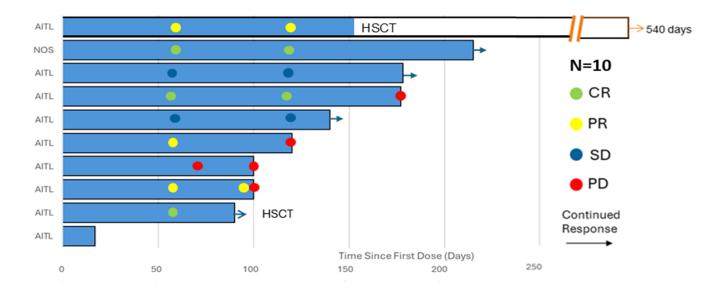
Stages 1 + 2 data shows high response rate in 2L EBV+ PTCL patients with a median DoR that has not yet been reached

Peripheral T-cell Lymphoma¹ (Overall Survival)



PTCL EBV+ Rate: 40-65%

60% ORR From NAVAL-1 Stages 1 + 2 in 2L EBV+ PTCL





Updated Nana-val Clinical Trial Plans in Patients with R/R EBV+ PTCL

Based on FDA Feedback and Robust NAVAL-1 Trial Stages 1 + 2 Clinical Responses

Feedback from meeting with FDA – important factors for accelerated approval NDA:

- Compelling ORR (and DOR)
- Randomized controlled trial (RCT) well underway at time of NDA submission



Robust clinical responses observed in 2L EBV+ PTCL patients from NAVAL-1 Trial Stages 1 and 2:

- 60% ORR (intent-to-treat)
- 67% ORR (efficacy-evaluable)

Best positioning for NDA submission – 4 potential opportunities:

- NDA filing in 2026 for accelerated approval
- 3 potential alternative opportunities



Updated Nana-val Clinical Trial Plans in Patients with R/R EBV+ PTCL

Four opportunities for potential NDA submission (1st of 2 slides)

Incorporating Data and FDA Feedback, Plan to Bring Forward Initiation of RCT While Continuing

NAVAL-1 Trial

A. Based on NAVAL-1 outcomes: Continue 120-patient **NAVAL-1** post-Stage 2 R/R (2L+) EBV+ PTCL expansion cohort with focus on **2L EBV+ PTCL**

- Reapproach FDA for potential accelerated NDA submission based on compelling ORR with mDOR ≥6 months and provided that RCT is well underway
 - (1) After 40 2L EBV+ PTCL patients enrolled and followed for at least 6 months at interim analysis, or
 - (2) After 120 **2L+ EBV+ PTCL** patients enrolled and followed for at least 6 months at **final analysis**
- Preserves opportunity for full approval in Japan following successful PMDA meeting
- (1), (2) indicate opportunities for potential NDA submission



Updated Nana-val Clinical Trial Plans in Patients with R/R EBV+ PTCL

Four opportunities for potential NDA submission (2nd of 2 slides)

Incorporating Data and FDA Feedback, Plan to Bring Forward Initiation of RCT While Continuing

NAVAL-1 Trial

- **B. Based on RCT outcomes:** Nana-val vs. investigator's choice available therapy in 120 patients (n=60 per arm) with **2L EBV+ PTCL**
 - Plan interim analysis of ORR after 60 patients (n=30 per arm) enrolled and followed for at least 6 months
 - (3) Plan accelerated NDA submission if statistically significant ORR improvement with mDOR ≥6 months and favorable safety profile
 - Plan final analysis of PFS after 120 patients with 2L EBV+ PTCL (n=60 per arm) enrolled and followed for at least 6 months
 - (4) Plan full NDA submission if statistically significant improvement in PFS supported by secondary endpoints
 - (3), (4) indicate opportunities for potential NDA submission



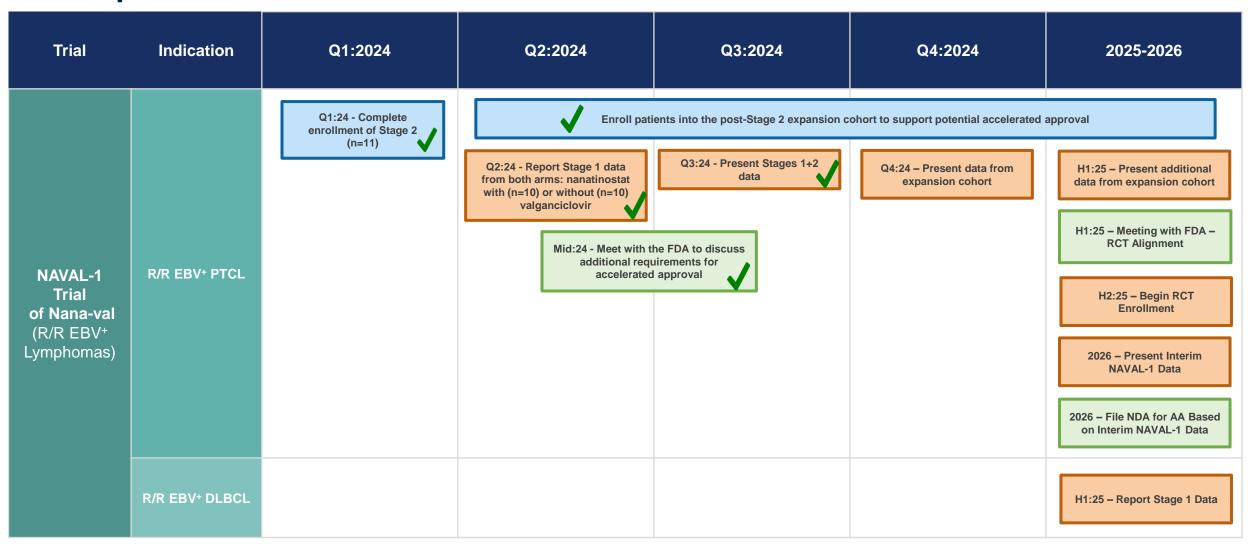
Nana-val Compares Favorably to Other Therapies that Received Accelerated Approval for the Treatment of R/R PTCL

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)	60-67% (2L) 33-41% (2L+)	25.8%	26.2%	26.6%
Complete Response Rate (CRR)	30-33% (2L) 19-24% (2L+)	10.8%	15.4%	8.3%
Duration of Response (DoR)	Not yet reached	8.4 months	<8.5 months	9.4 months
Registration Sample Size	40 (IA) 120 (FA)	120	130	109
Route of Administration	Oral	IV	IV	IV





Anticipated 2024-2026 Milestones





Related Strategic and Resource Prioritization Actions

- Pausing development of solid tumor program after RP2D determination in 2H:24
- Reduction in force of ~23% of company's employees in August 2024

Focus is Maximizing the Nana-val Opportunity









Adverse survival outcomes are seen with many EBV-associated cancers

High unmet medical need for targeted therapies

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

First-in-class targeted treatment; potential tumor agnostic MOA

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

Positive Stages 1 + 2 PTCL
efficacy data particularly in
second-line patients

FDA interaction provides clarity on regulatory path

Potential for NDA filing for accelerated approval in 2026; fast track designation & 7 orphan drug designations





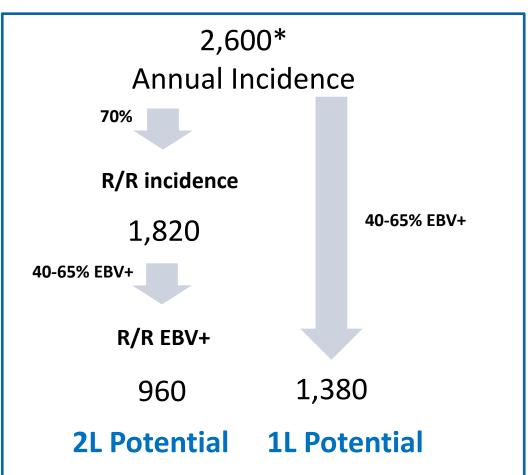
Questions and Answers



US EBV+ PTCL Market Opportunity*



Patients

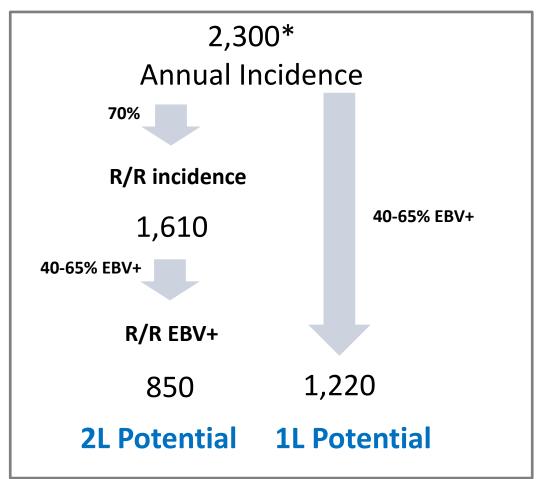


Other Key Drivers

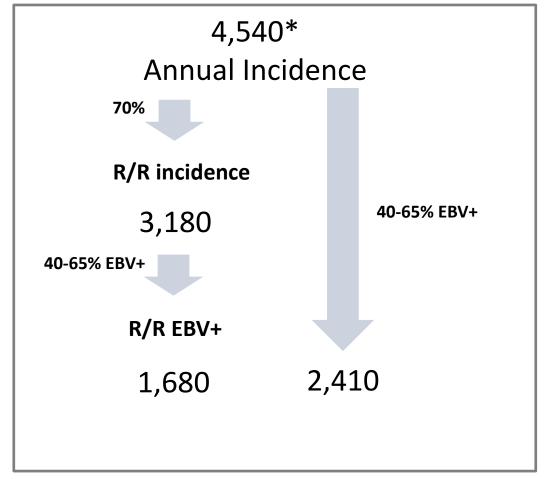
Response rate	60% ITT in 2L
Pricing Considerations	No standard of care for second line Low 5-year survival (11%) Strong preliminary Nana-val data
Line of Therapy	Potential 2L → 1L
Duration of Response	Current therapies: 4-8 months*** Nana-val: 17.3 months (201 study)** NAVAL-1 mDOR not yet reached
Market Penetration	Effective, well tolerated, targeted, easy to use (outpatient oral therapy).
EBV Testing Rate	Testing encouraged by guidelines Nana-val availability will drive testing

Japan and Europe EBV+ PTCL Market Opportunity*











Summary of Addressable PTCL Patients for Major Markets

			* * * *	Total
Incidence	2,600	2,300	4,540	9,440
R/R	1,820	1,610	3,180	6,610
1L EBV+	1,380	1,220	2,410	5,010
2L EBV+	960	850	1,680	3,490

Actual number of EBV-positive cases likely underreported due to inconsistent EBV testing in the absence of an actionable EBV-targeted therapy

Includes PTCL-NOS and AITL. For big 5 EU (includes UK), extrapolated for total EU.

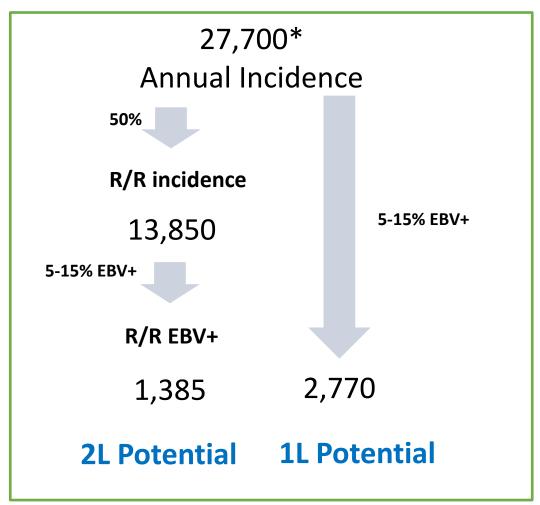
Tessellon, SEER Stat database, NVS/FRANCIM Cancer Registry, Cancer Research UK, Robert Koch Institute, Japan national Cancer Center



US EBV+ DLBCL Market Opportunity



Patients



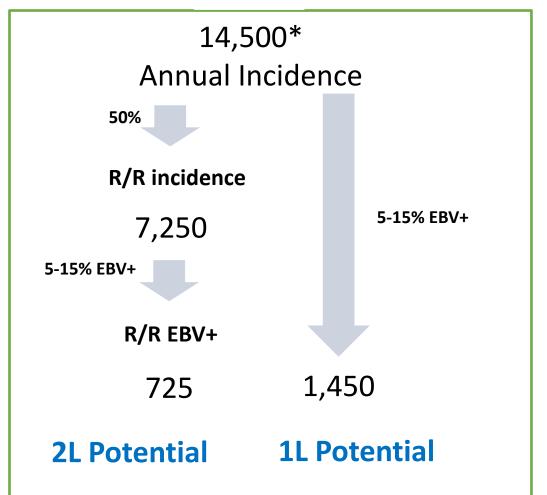
Other Key Drivers

Response rate	ORR = 67%, CR = 33%
Pricing Considerations	Separate EBV+ WHO classification Low 5-year survival Strong preliminary Nana-val data
Line of Therapy	Potential 2L → 1L
Duration of Response	DoR >12 months considered clinically meaningful** DoR for Nana-val not yet calculated, multiple patients still on long-term therapy (ranging from 11-42 months)*
Market Penetration	Effective, well tolerated, targeted, easy to use (outpatient oral therapy).
EBV Testing Rate	Opportunity to drive awareness Nana-val availability will drive testing

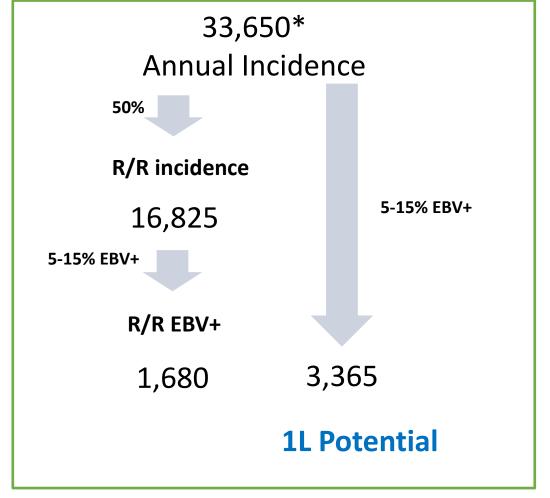


Japan and Europe EBV+ DLBCL Market Opportunity











Summary of Addressable DLBCL Patients for Major Markets

			* * * * * * * * * * * * * * * * * * *	Total
Incidence	27,700	14,500	33,650	75,850
R/R	13,850	7,250	16,825	37,925
1L EBV+	2,770	1,450	3,365	7,585
2L EBV+	1,385	725	1,680	3,790

Actual number of EBV-positive cases likely underreported due to inconsistent EBV testing in the absence of an actionable EBV-targeted therapy

For big 5 EU (includes UK), extrapolated for total EU.
Tessellon, SEER Stat database, NVS/FRANCIM Cancer Registry, Cancer Research UK, Robert Koch Institute, Japan national Cancer Center

