AOS 2025
Connect and Collaborate to Conquer Cancer

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Early Clinical Outcome of VRN110755 in NSCLC Patients with EGFR Mutations

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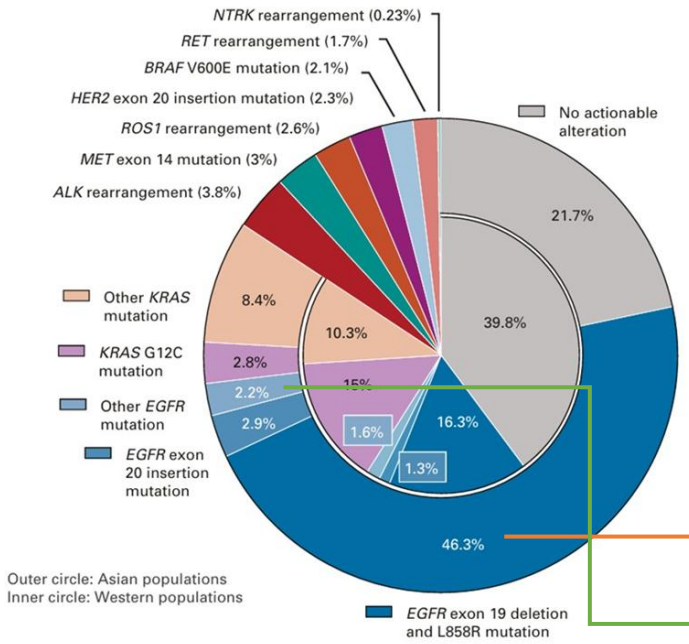
(Voronoi Inc., South Korea)

COI Disclosure Information

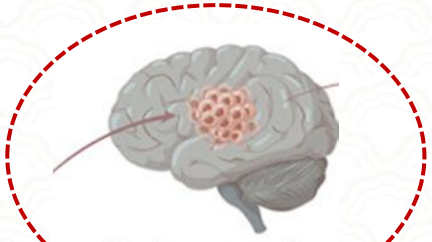
I have financial relationships to disclose.

Employee of Voronoi Inc.

EGFR-driven NSCLC



Tan AC and Tan DSW, 2022 J. Clinical Oncology



Classic drivers
L858R or Del19

1/2G EGFR TKI

3G EGFR TKI
(Osimertinib)

Resistant mutations

+T790M mutation
(DT or LT)

+C797S mutation
(DC or LC)

Atypical drivers
compound mutations

1/2/3G EGFR TKI

- In Asia, more than 50% of NSCLC patients have EGFR activating mutations.

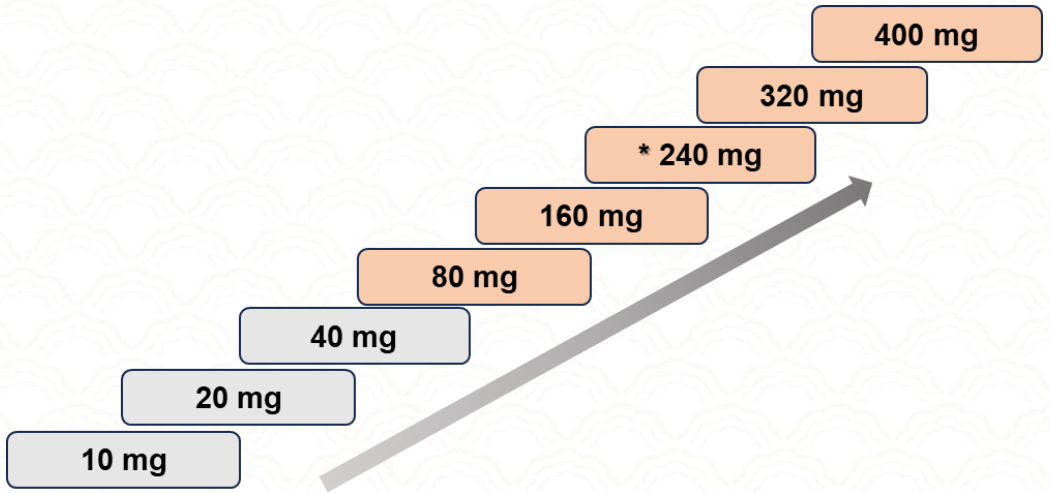
- T790M and C797S are acquired resistant mutations against 1/2G EGFR TKI and 3G EGFR TKI, respectively.
- An unmet need remains for well-tolerated and brain-permeable oral therapies with clinical benefit against common and uncommon EGFR driver mutations.
- VRN110755, a Novel class of EGFR TKIs with high potency against common, uncommon, and acquired resistance mutations, along with high brain permeability.

VRN110755 Phase 1 Dose Escalation Study

Key Eligibility Criteria

- Aged ≥ 18
- ECOG PS 0-1
- Advanced NSCLC with EGFR common or uncommon driver mutations
- Failed standard treatment
- Active brain metastasis allowed

Dose Escalation (3+3) and Backfill

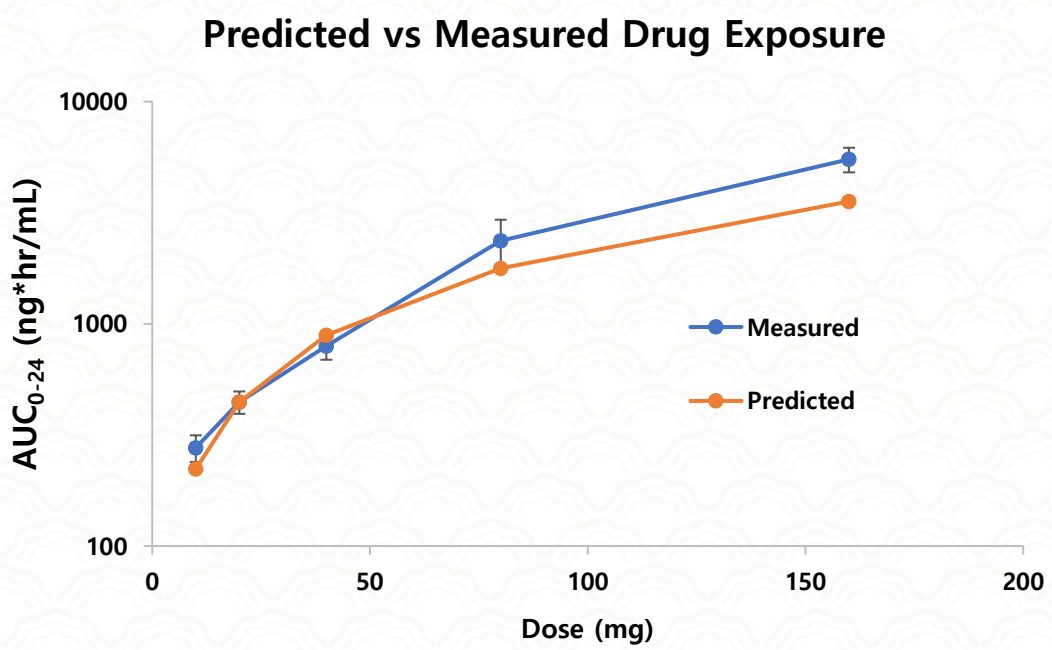


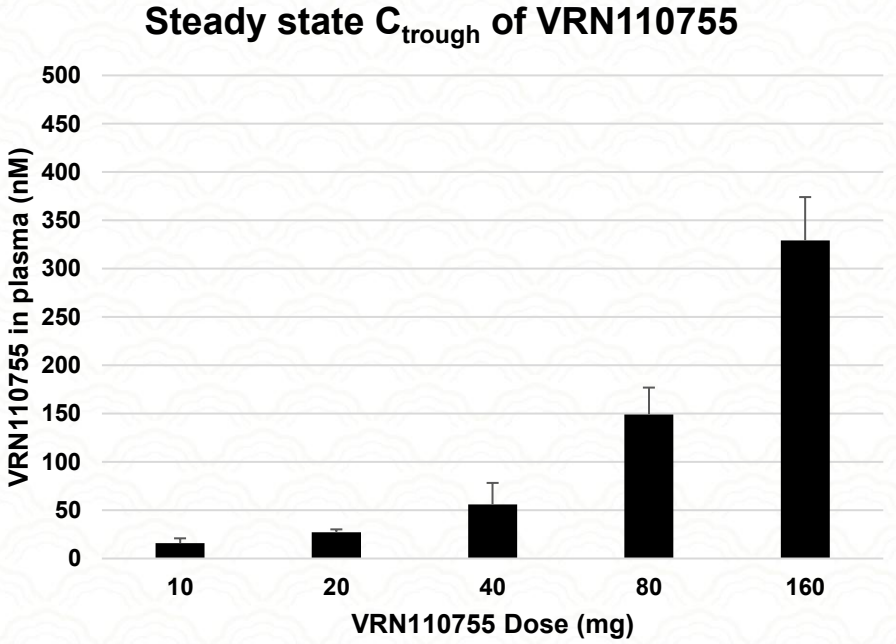
Key Endpoints

- Safety and tolerability
- Pharmacokinetics
- Anti-tumor responses

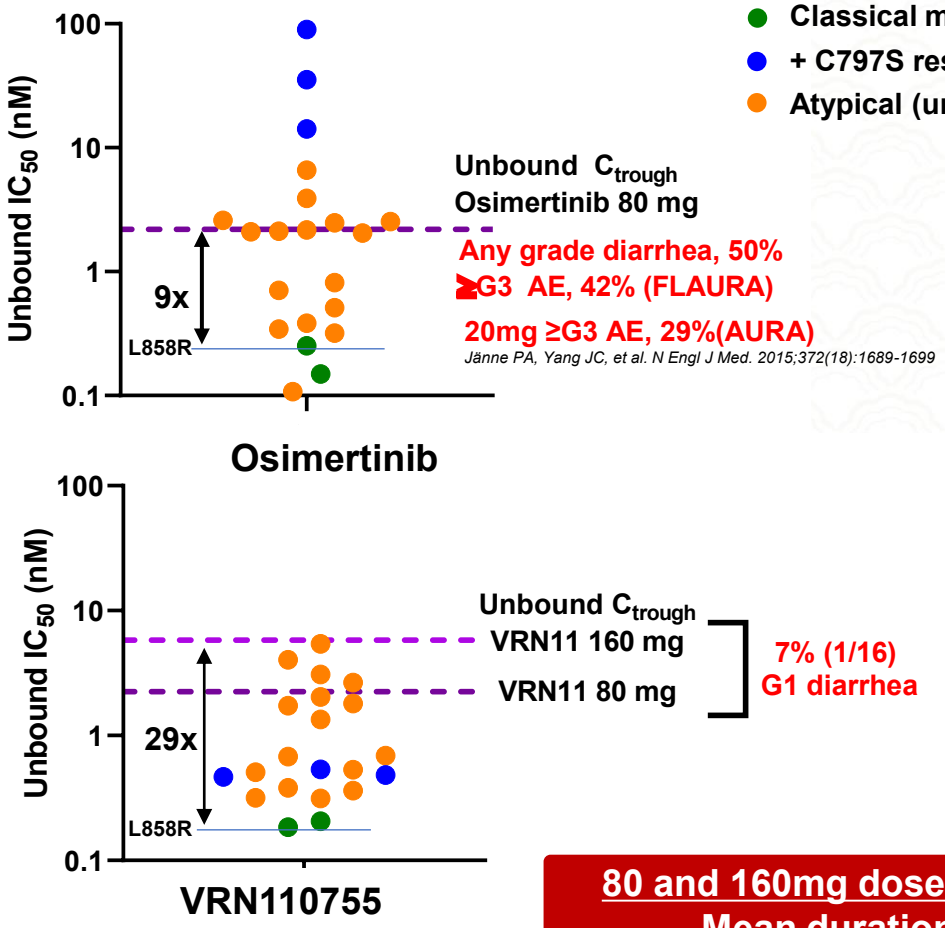
Pharmacokinetics of VRN110755

VRN110755 human PK was well translated from preclinical studies, showing a dose-proportional increase in AUC and C_{trough}



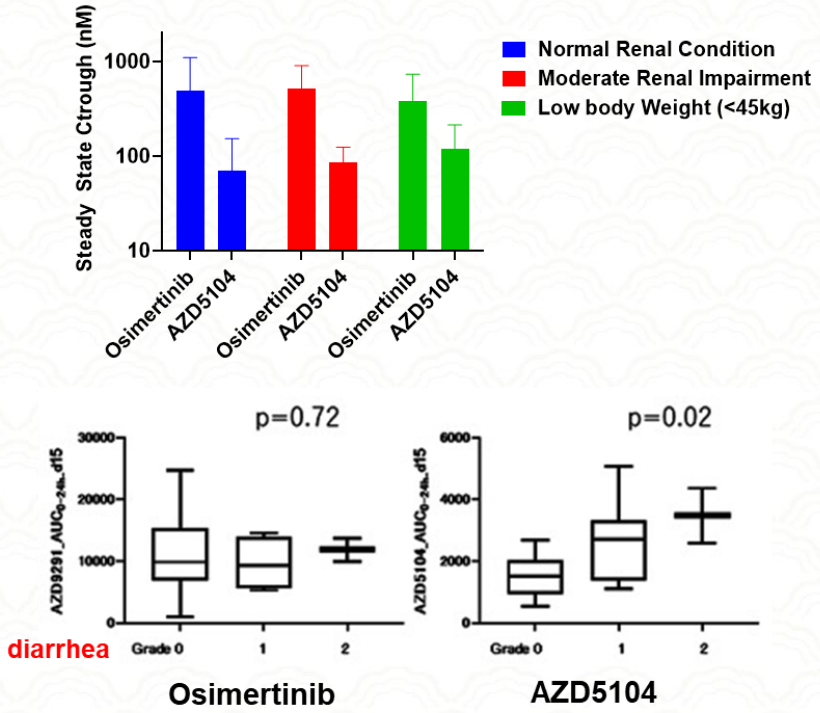


Target engagement from 40 mg



80 and 160mg dosed patients (n=16)
Mean duration: 10 weeks
(2~27 weeks, as of 2025.06)

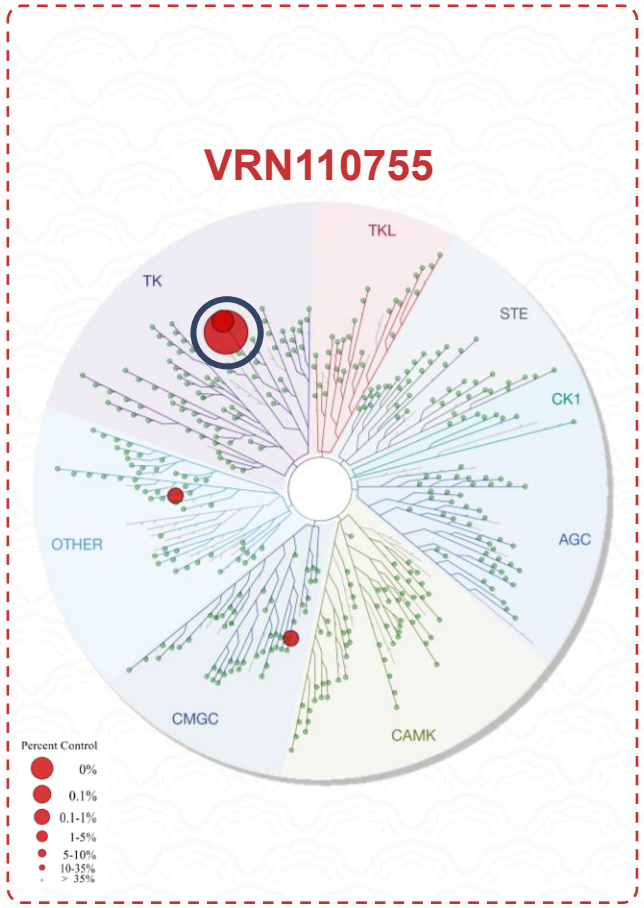
Active metabolite (AZD5104)-related diarrhea

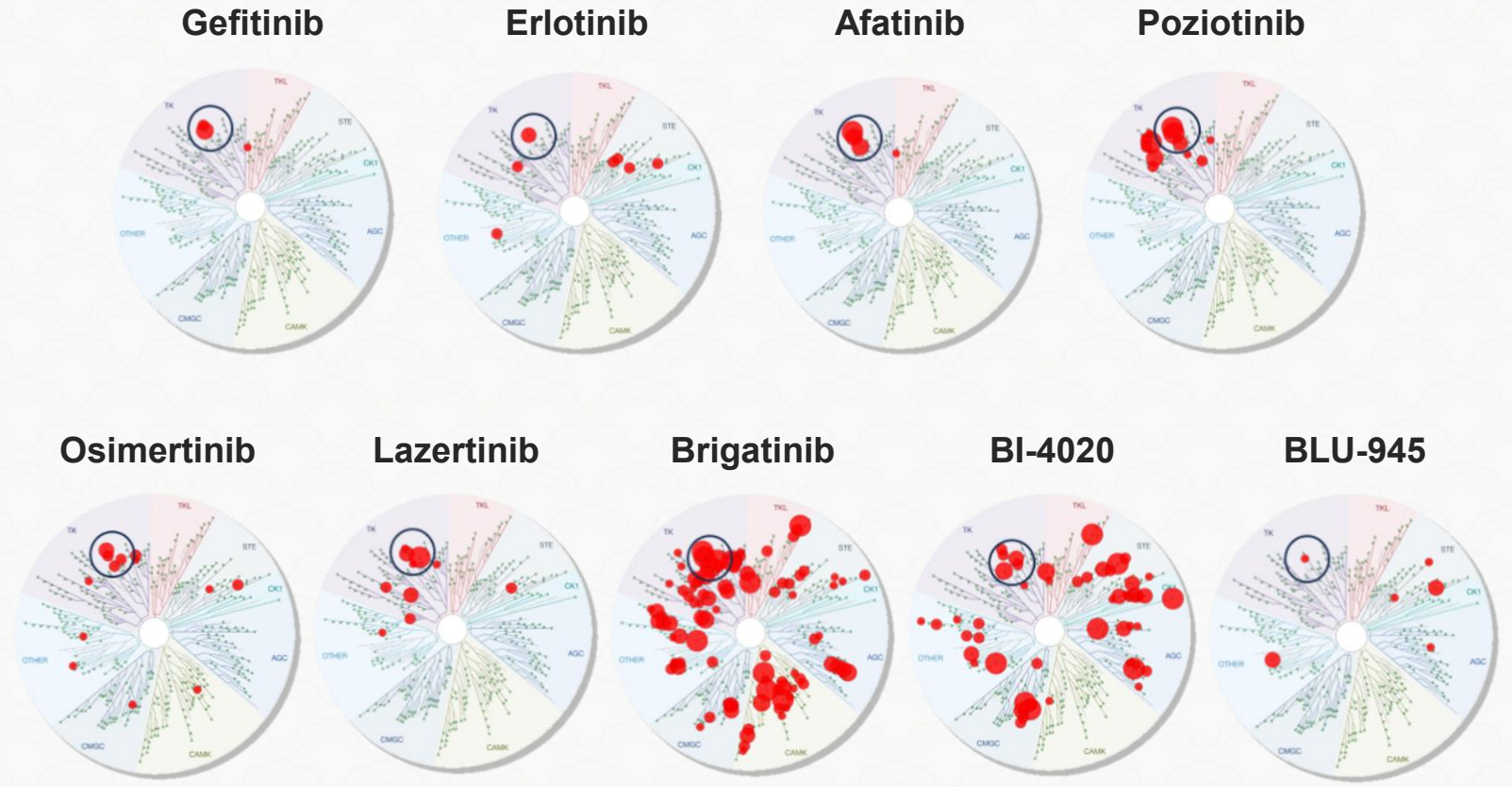


Fujiwara Y, et al., Cancer Sci. 2023 May;114(5):2087-2097.

Target selectivity and fewer off-target kinases

Kinome profiles showed that VRN110755 is highly selective to the ERBB family, without significant off-target kinase. Fewer off-target mediated AEs are expected.



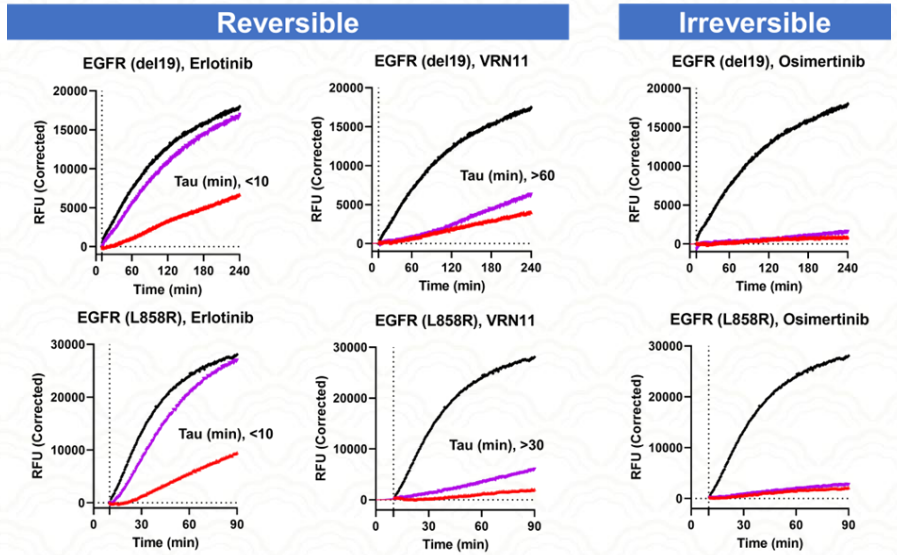


In vitro to clinic translation, potency and efficacy

		Driver Del19	Driver L858R	Resistance T790M	Resistance C797S	Atypical/ Uncommon	Brain permeability
1 Generation Non-covalent	Erlotinib Gefitinib	+++	+++	-	+	+	-
2 Generation Covalent to C797	Afatinib Dacomitinib	+++	+++	+	-	++	-
3 Generation Covalent to C797	Osimertinib Lazertinib	+++	+++	+++	-	++	++
1/4 Generation Non-covalent	VRN110755	+++	+++	++	+++	+++	+++

VRN110755 is non-covalent, but has a long target residency, unlike prior 1G non-covalent inhibitors, promising high potency

In vitro



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1/4 Generation Non-covalent	VRN110755	+++	+++	++	+++	+++	+++

In vitro

Catalytic IC_{50} (nM)	Driver	Resistance		Uncommon		
TKI	Del19	Del19-T790M	Del19-C797S	L861Q	G719S	L718Q
1G Erlotinib	3	1,390	<1.0	<1.0	2	34.1
3G Osimemrtinib	2.8	0.8	240	<1.0	10.3	292
VRN110755	3.6	7.1	<1.0	<1.0	<1.0	3

High potency against common, uncommon and resistant EGFR mutants

In vitro to clinic translation, potency and efficacy

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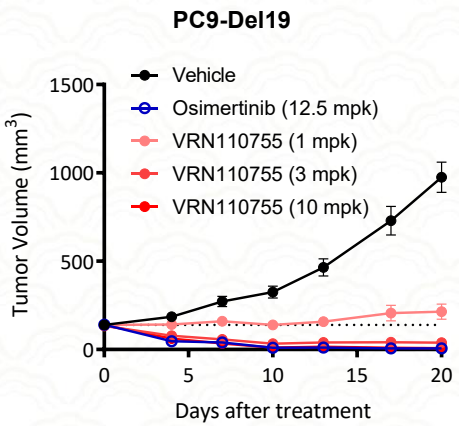
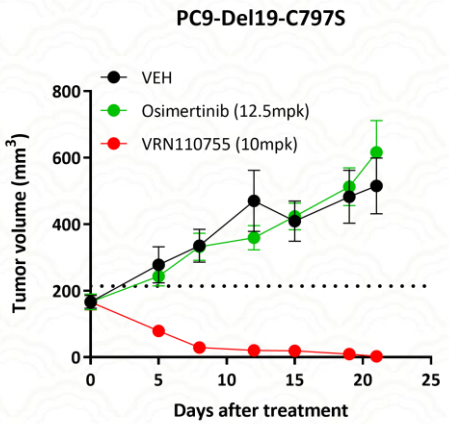
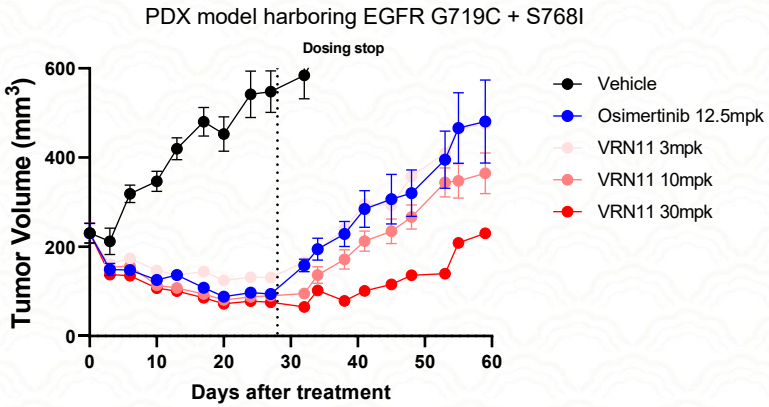
In vivo







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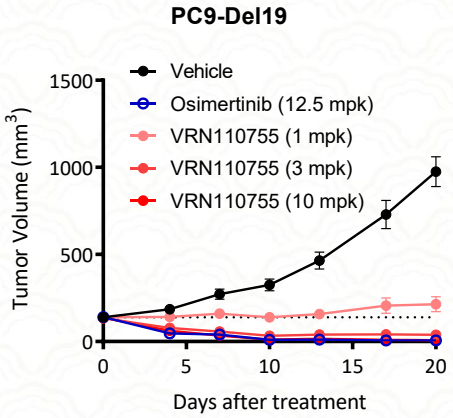
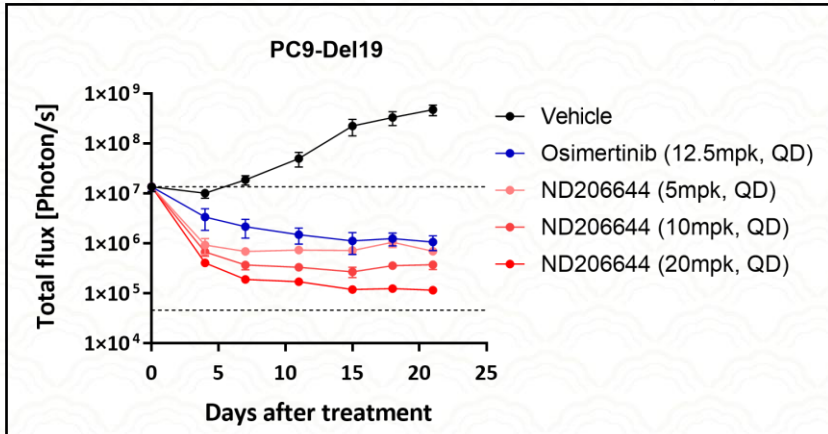
In vivo





	Osimertinib	VRN110755
Mouse $K_{puu\ brain}$	0.3[1]	0.4 ~ 0.6
Rat $K_{puu\ brain}$	0.21[3]	0.6
Monkey BP ratio	4.2[3]	29.4
$K_{puu\ brain}$	NA	1.7
$K_{puu\ csf}$	NA	2.7

In vitro to clinic translation, potency and efficacy

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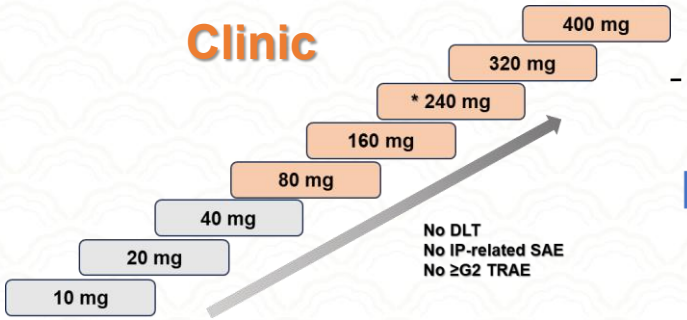

80 mg, Patient with EGFR^{Del19} NSCLC

Baseline and VRN110755 Treatment

- ✓ EGFR-Del19 and TP53 mutation at the baseline
- ✓ Two prior systemic treatments, including **afatinib**
- ✓ 80 to 160 mg QD, > 27 weeks (on treatment)
- ✓ **Lung lesions, ~ 34% reduction (after 4 weeks)**
- ✓ Pleural effusion: disappearance
- ✓ EGFR ctDNA VAF(%): 0.1 to 0 after 2 cycles
- ✓ **Best response: PR**
- ✓ Safety: G1 skin rash, G1 LLE

160 mg, Patient with EGFR^{Del19} NSCLC

Baseline and VRN110755 Treatment

- ✓ EGFR-Del19 and brain metastasis at the baseline
- ✓ Prior treatment: **Osimertinib (disease progression after 5 months)**
- ✓ **Target lesions, ~ 7% reduction (after 4 weeks)**
- ✓ Best response: SD (including brain lesion)
- ✓ **Safety: no TRAE**

240 mg, Patient with EGFR^{L858R} NSCLC

Baseline and VRN110755 Treatment

- ✓ EGFR L858R mutation at the baseline
- ✓ Prior treatment: 10 prior treatments
- ✓ **Target lesions: 43% reduction (after 4 weeks)**
- ✓ Best response: **PR**
- ✓ Safety: G1 skin rash

In vitro to clinic translation, potency and efficacy

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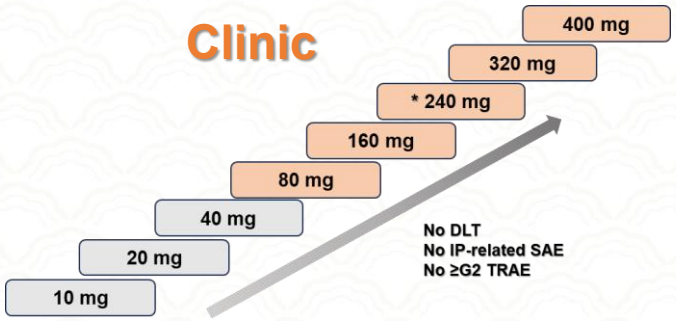
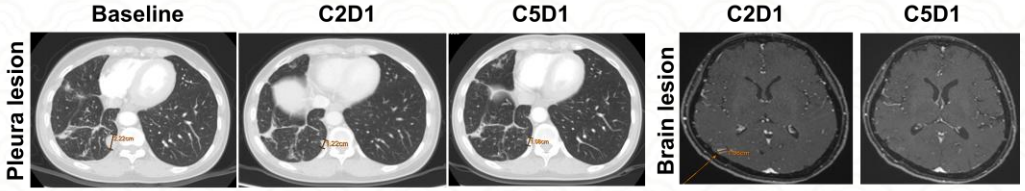


Primary efficacy population

40 mg, Patient with $EGFR^{L858R/R776H/C797S}$ NSCLC

Baseline and Treatment History	VRN110755 Treatment
✓ Lung, brain, and pleural metastasis	✓ 40 mg QD, 19 weeks
✓ $EGFR^{L858R/R776H/C797S}$ at the baseline	✓ **Pleura lesion: 51% tumor reduction**
✓ Two prior systemic treatments, including **dacomitinib and osimertinib**	✓ **CNS lesion: tumor disappearance**
	✓ EGFR ctDNA VAF(%): 0.3 to 0 after 2 cycles
	✓ **Best response: PR**
	✓ Safety: grade 1 malaise TRAE



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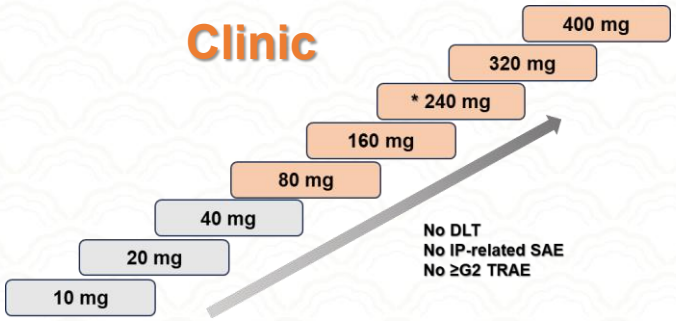


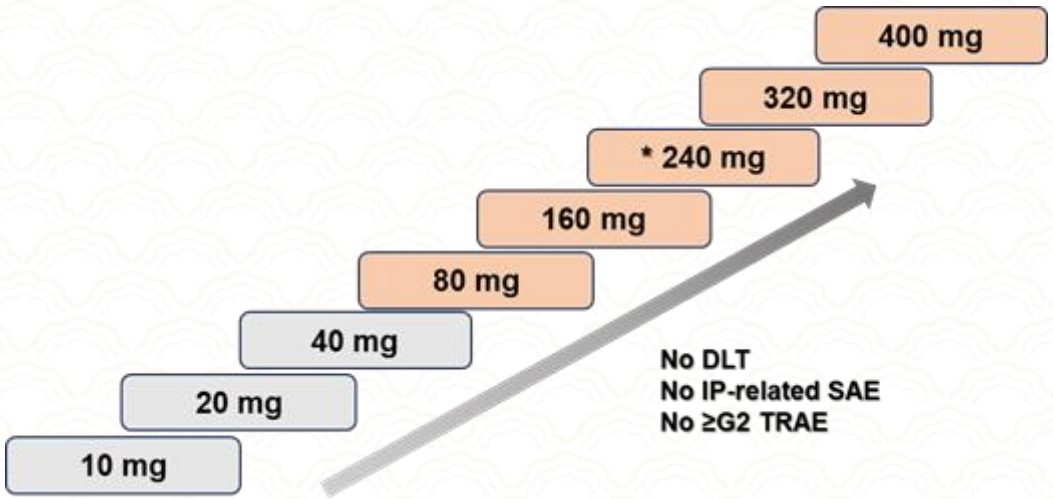
3 patients with T790M positive at baseline (80/160mg)
All patients showed shrinkage of the target lesion tumor,
One patient showed >10% tumor shrinkage

VRN110755 Phase 1 Dose Escalation Study

Key Eligibility Criteria

- Aged ≥ 18
- ECOG PS 0-1
- Advanced NSCLC with EGFR common or uncommon driver mutations
- Failed standard treatment
- Active brain metastasis allowed

Dose Escalation (3+3) and Backfill



Key Endpoints

- Safety and tolerability
- Pharmacokinetics
- Anti-tumor responses

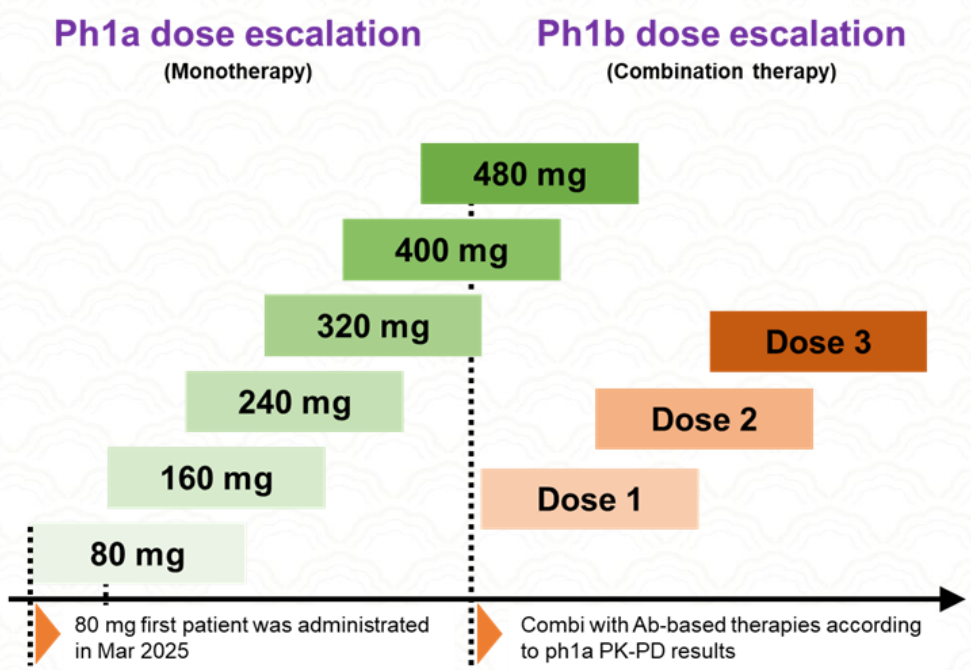
Recommended doses will be selected for the expansion/extension studies with efficacy populations and combination studies with chemotherapies.

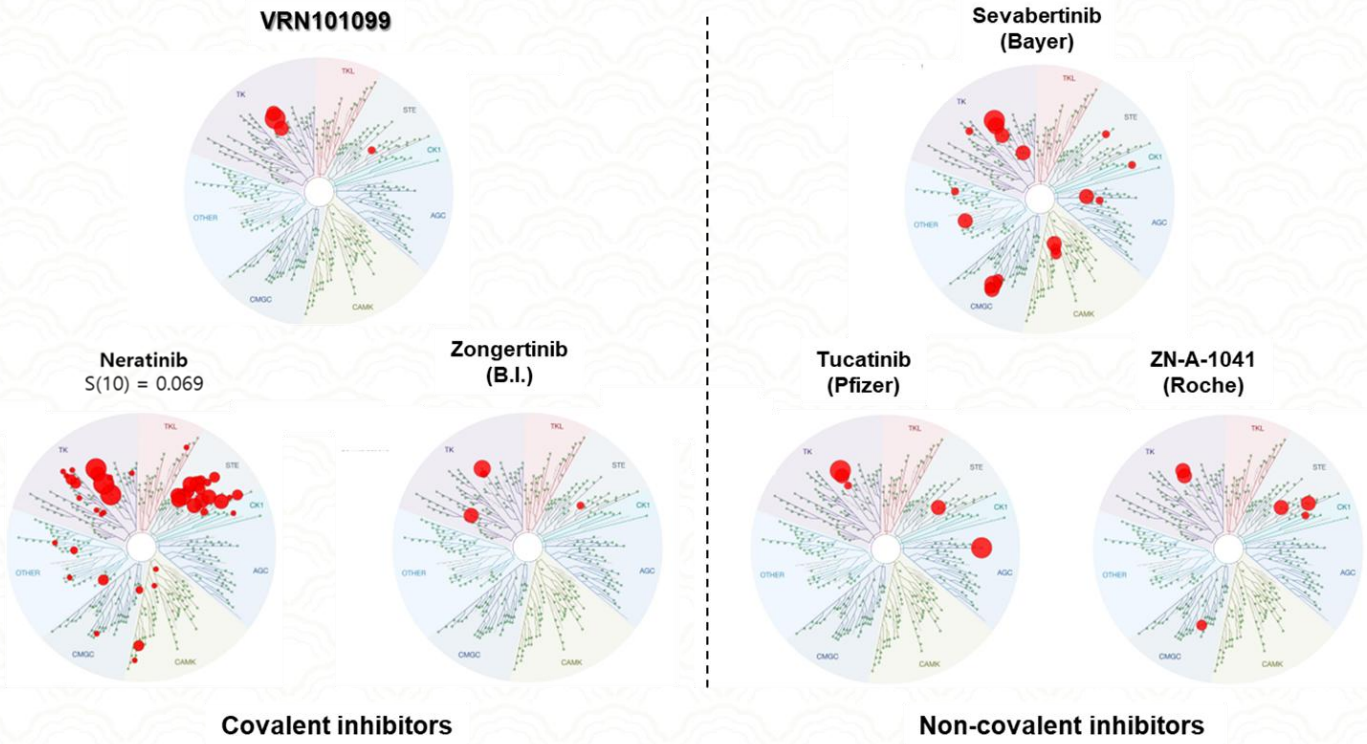
Acknowledgements

- The patients and their families/caregivers
- Investigators, nurses, and staff at all sites.
- Medical team of Voronoi Inc.

VRN101099, HER2 covalent inhibitor

Phase 1a, dose escalation with HER2+ or HER2m solid tumor



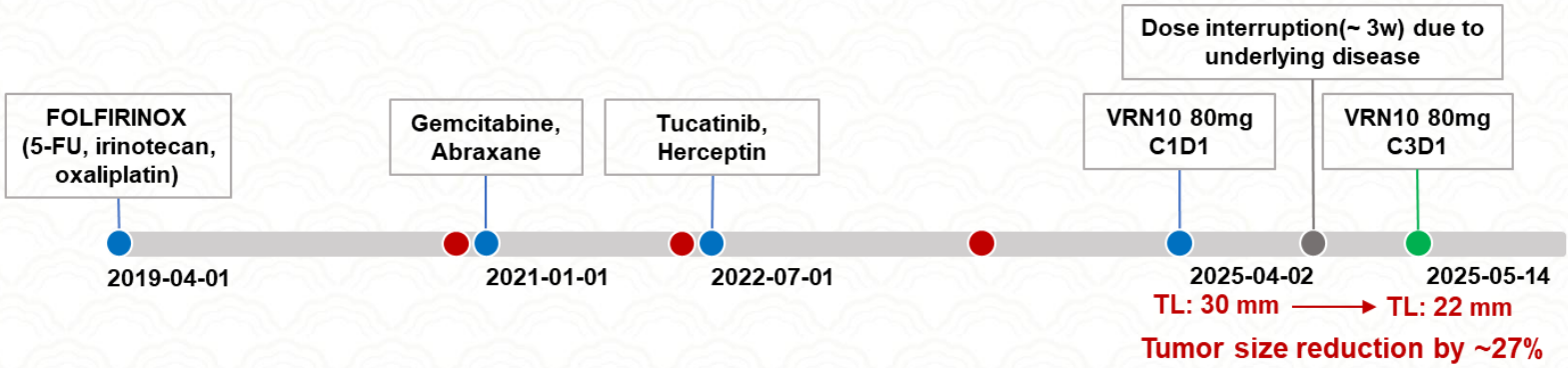


VRN101099, HER2 covalent inhibitor

Phase 1a, dose escalation with HER2+ or HER2m solid tumor

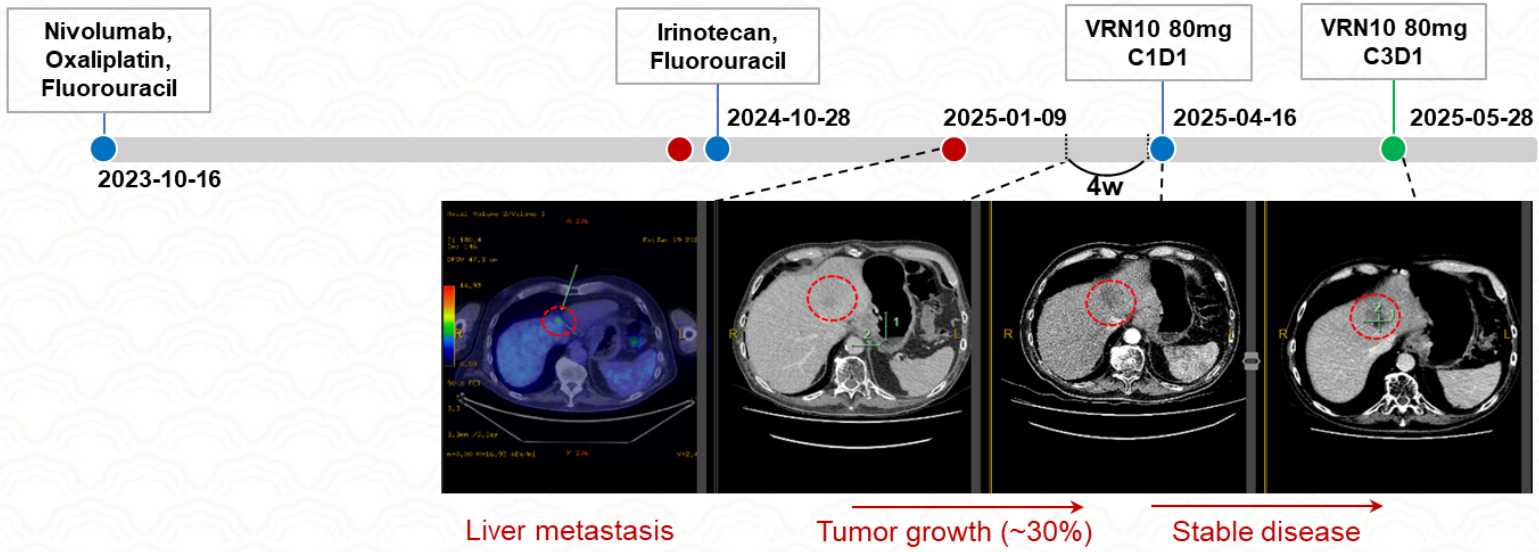
VRN101099 80mg, Pancreas (AU001-001)

- HER2-S310F mutation, Pancreas
- Target Lesion: Gastrointestinal tract(GI) 30mm
- Tumor Assessment: (C3D1) Stable disease



VRN101099 80mg, Gastric (AU002-003)

- HER2: IHC 2+ / DISH-, Gastric
- Target Lesion: Gastroesophageal junction (GEJ) 42mm , Liver metastasis 40mm
- Tumor Assessment: (C3D1) Stable disease
- Cycle 4 ongoing



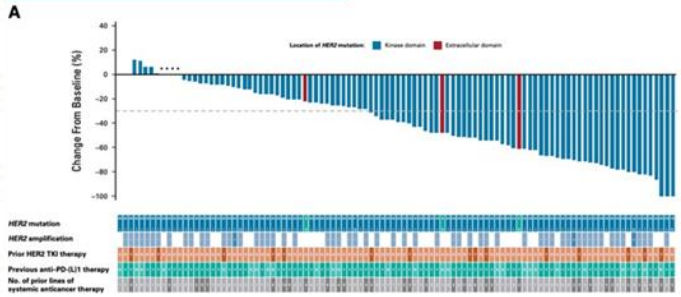
VRN101099, HER2 covalent inhibitor

Phase 1a, dose escalation with HER2+ or HER2m solid tumor

TRAEs, n (%)	120 mg n = 75		240 mg n = 57	
	All	Grade ≥3	All	Grade ≥3
Any TRAE*	69 (92)	13 (17)	57 (100)	11 (19)
Diarrhea	36 (48)	1 (1)	37 (65)	1 (2)
Rash†	18 (24)	0	17 (30)	0
ALT increased	14 (19)	6 (8)	16 (28)	6 (11)
AST increased	16 (21)	4 (5)	14 (25)	4 (7)
Anemia	8 (11)	0	10 (18)	0
Nausea	10 (13)	0	4 (7)	0
Neutrophil count decreased	7 (9)	1 (1)	7 (12)	3 (5)
Pruritus	6 (8)	0	8 (14)	0
Serious TRAE	3 (4)	3 (4)	7 (12)	5 (9)

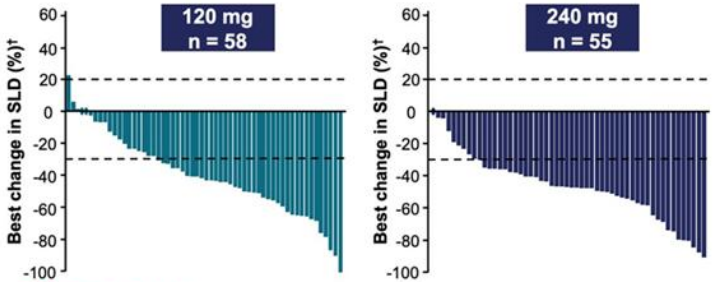
2024, WCLC

DESTINY-Lung 02
T-Dxd



ORR 49%
mPFS 9.9 months

Beamion LUNG-1
Zongertinib



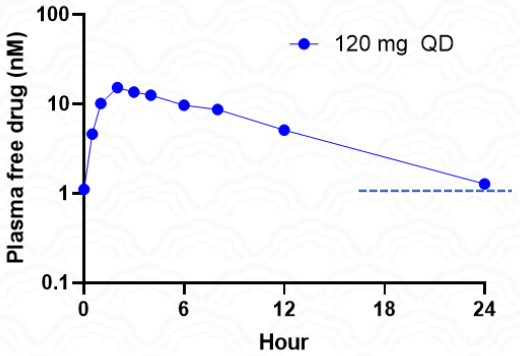
ORR 71%
mPFS 12.9 months

Corassa M, 2025, ASCO

VRN101099, HER2 covalent inhibitor

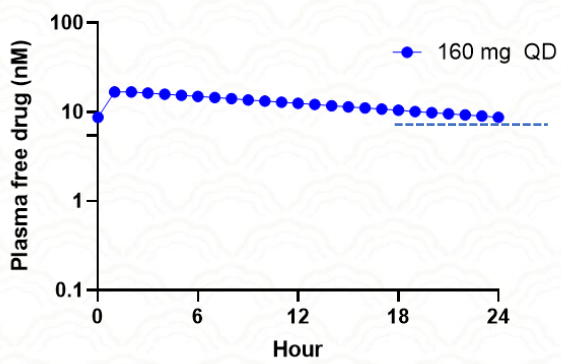
Phase 1a, dose escalation with HER2+ or HER2m solid tumor

Zongertinib, unbound PK

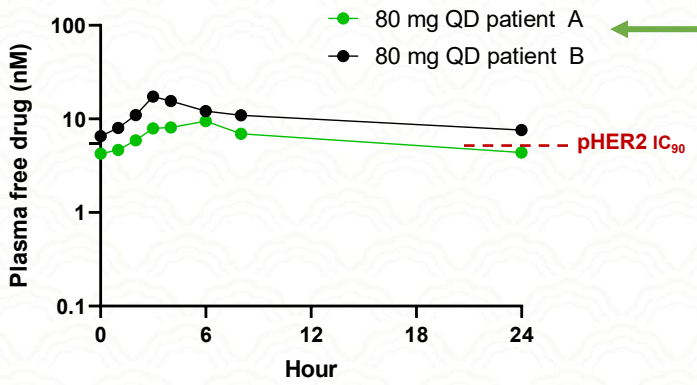


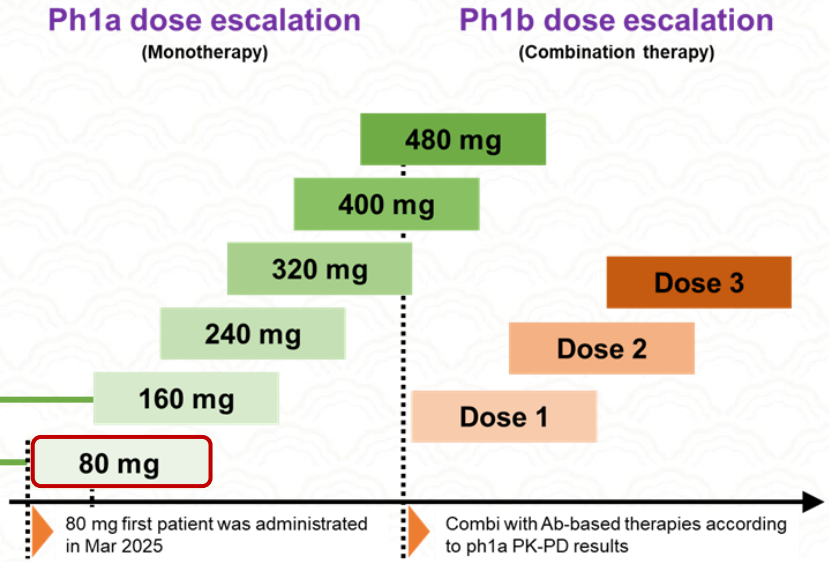
≥G3 TRAE(LLE, etc.), 17%
Any TRAE, 92%

VRN101099, expected unbound PK



VRN101099, unbound PK





First Cohort, 80mg (n=3)	
Efficacy	✓ A patient with HER2-S310F(Pancreas), **> 27% tumor size reduction** ✓ A patient with HER2 IHC2+(Gastric), **Tumor growth inhibition**
Safety	**No TRAE**