Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design

VORONOI

IR BOOK

February 2025

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VORONOI

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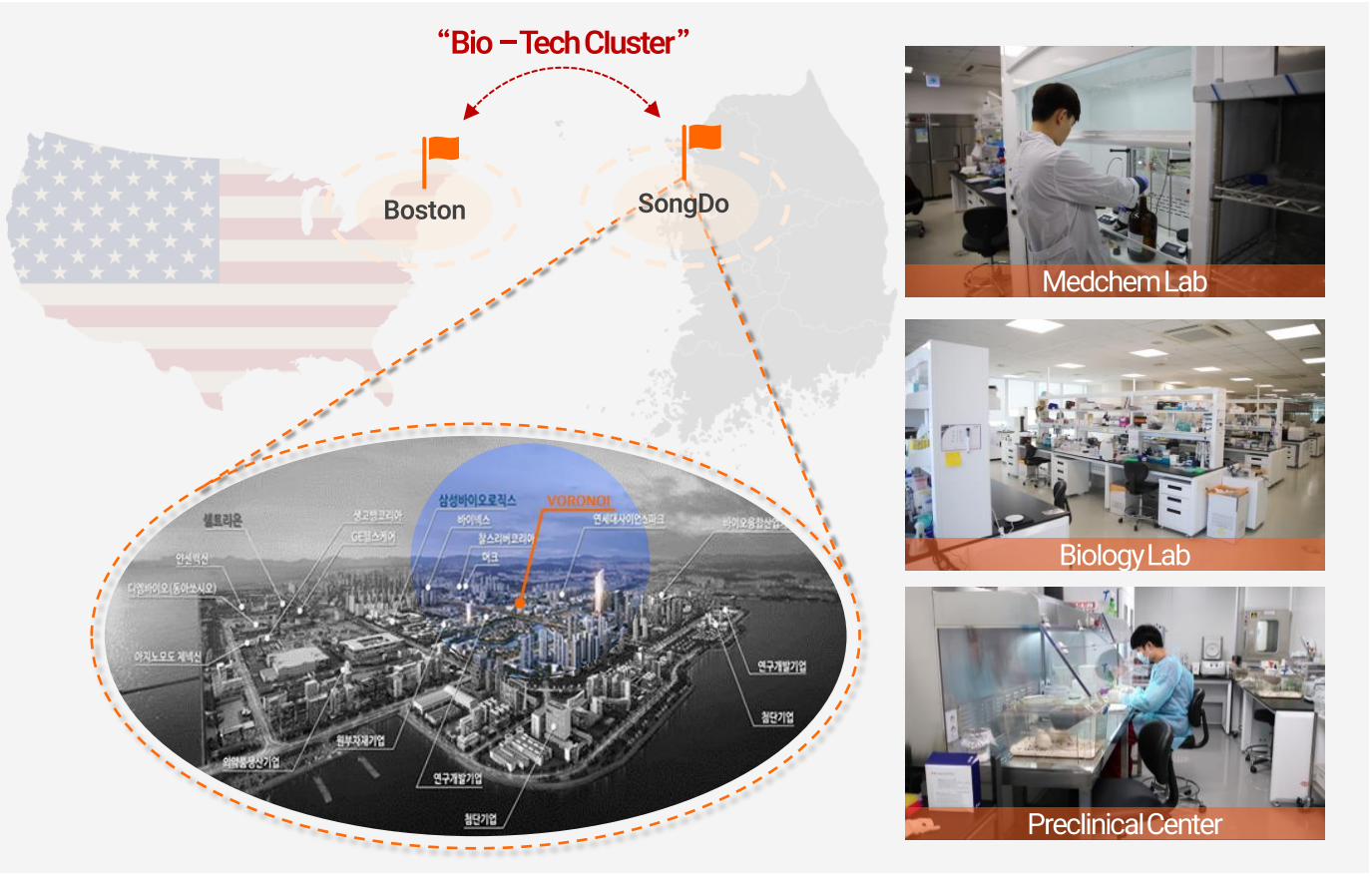
2. ORIC-114(VRN07). EGFR exon20 insertion NSCLC Targeted Therapy
3. VRN10. HER2+ Breast Cancer Targeted Therapy

VORONOI. Overview

Company Overview

Establishment	Feb 2015 (KOSDAQ IPO in Jun 2022)
Chief Executive Officer	Daekwon Kim, Hyuntae Kim
Headquarters	Bldg S 18F, Songdogwahak-ro 32, Yeonsu-gu, Incheon, Republic of Korea 21984
Business Overview	New Drug Development
Research Areas	Targeted Therapies for Oncology and Refractory Diseases
Employees (2024.4Q)	150
Capital (2024.3Q)	9.1 billion KRW
Assets (2024.3Q)	82.3 billion KRW

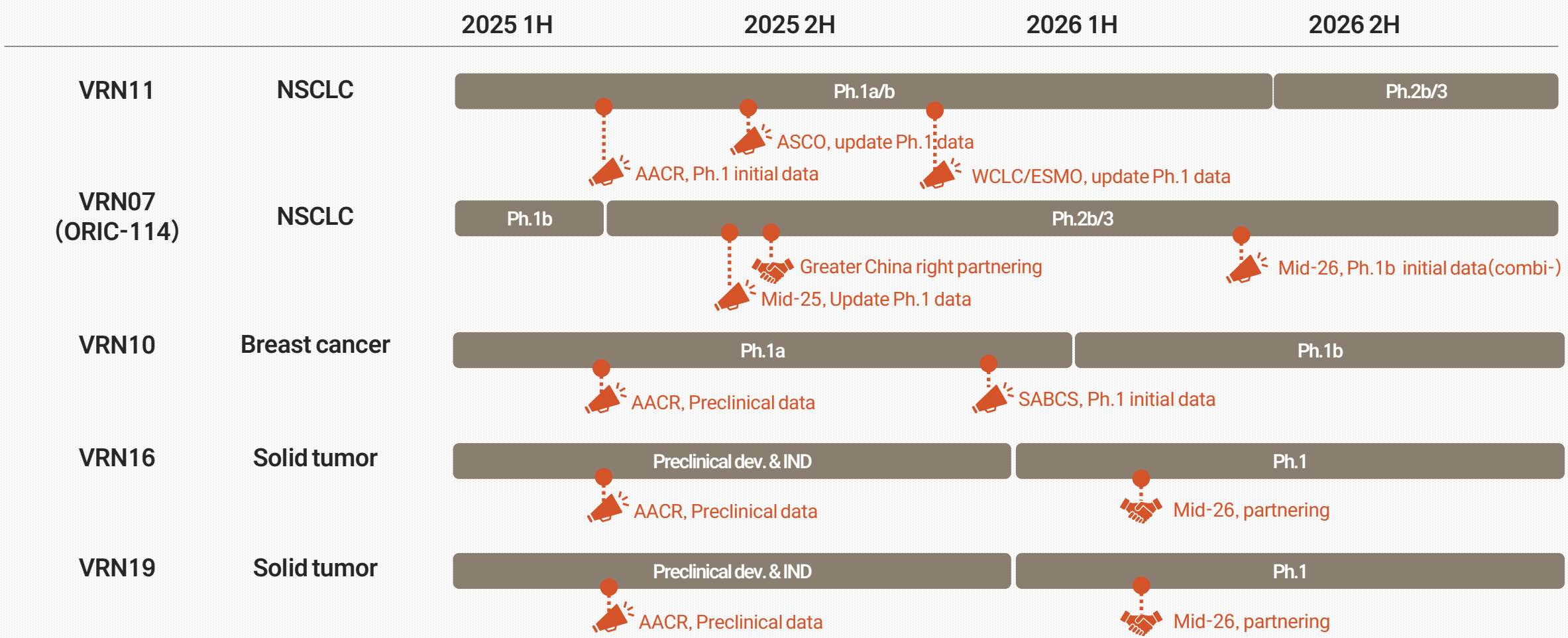
Company Structure

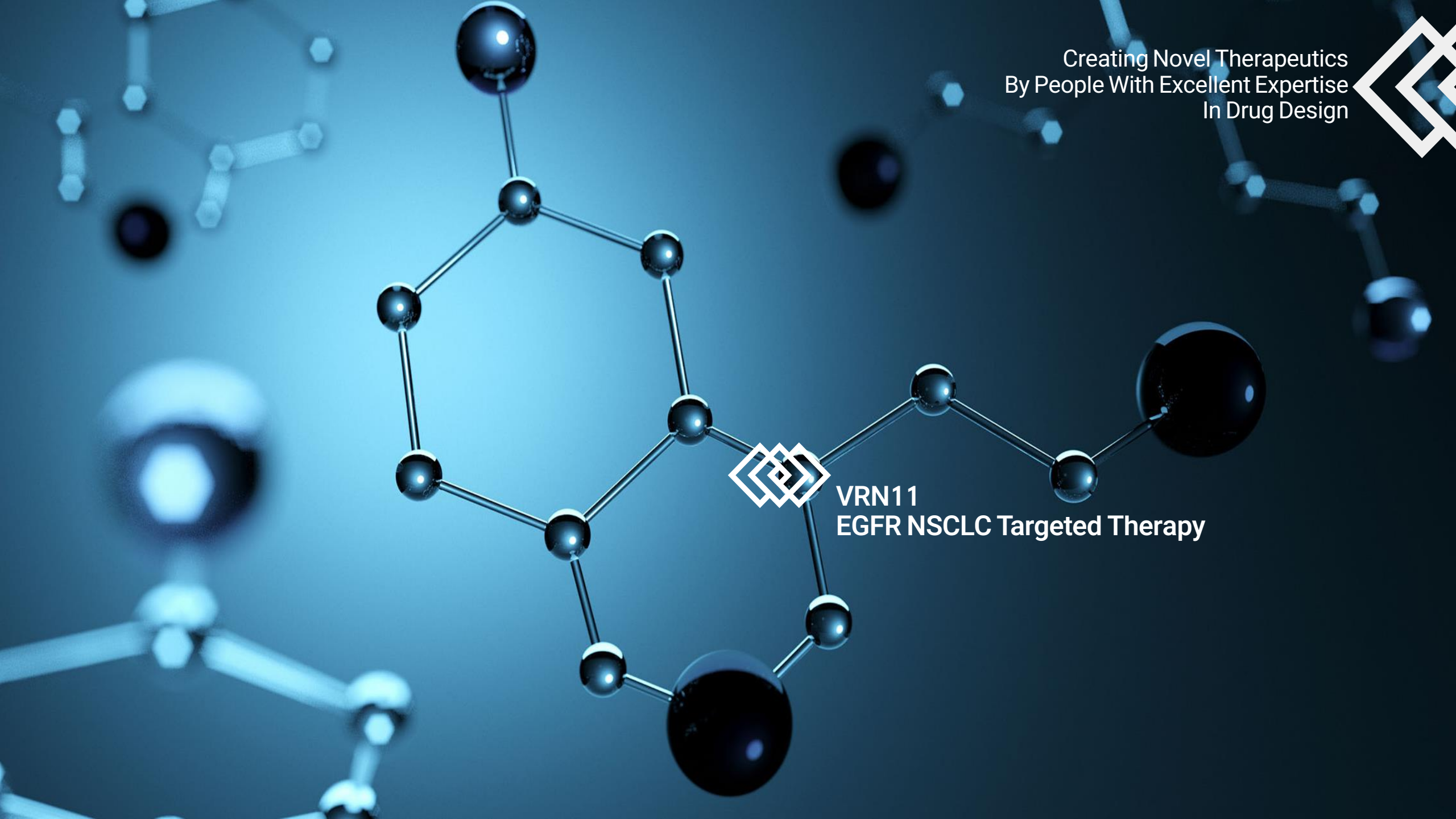


VORONOI. Pipeline

Drug	Company	Indication	Target	Clinical Phase
				Pre-clinical / Phase 1 / Phase 2 / Phase 3
VRN11	VORONOI	Non-small cell lung cancer (NSCLC)	EGFR del19/C797S, EGFR L858R/C797S	
			EGFR del19, EGFR L858R (Brain metastasis)	
			EGFR uncommon (2L setting)	
			EGFR del19, L858R, uncommon	
VRN07 (ORIC-114)	ORIC	NSCLC	EGFR exon20 ins (treatment-naïve)	
			EGFR exon20 ins (post-amivantamab)	
			EGFR exon20 ins (with SC amivantamab) Janssen Johnson&Johnson	
			EGFR uncommon	
			HER2 exon20 ins	
VRN10	VORONOI	Breast cancer	HER2+ positive	
VRN06	inno.N	Lung and thyroid cancer	RET fusion	
VRN04	Anvia Therapeutics	Auto-immune disease	RIPK1	
VRN13	VORONOI	Pulmonary arterial hypertension (PAH)	PDGFR	
VRN16	VORONOI	Solid Tumor	PKMYT1	
VRN19	VORONOI	Solid Tumor	USP1	

VORONOI. Milestone Guidance

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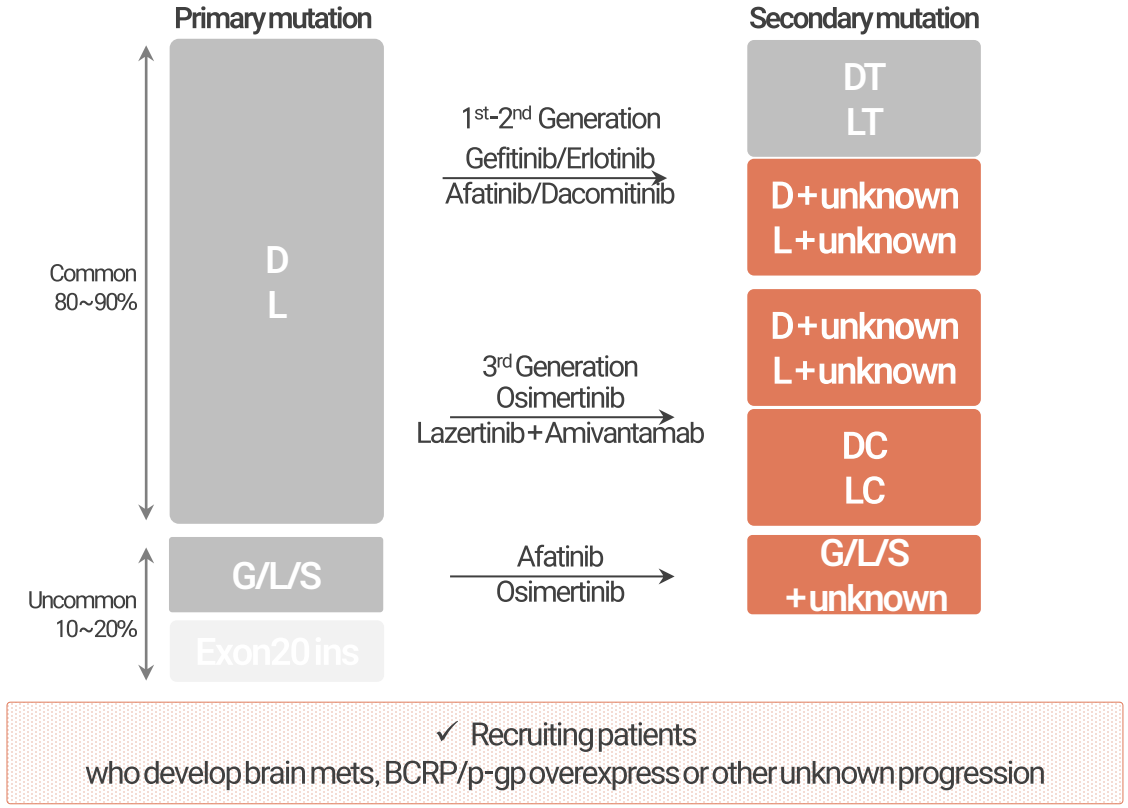
VRN11
EGFR NSCLC Targeted Therapy

VRN11. EGFR NSCLC Landscape

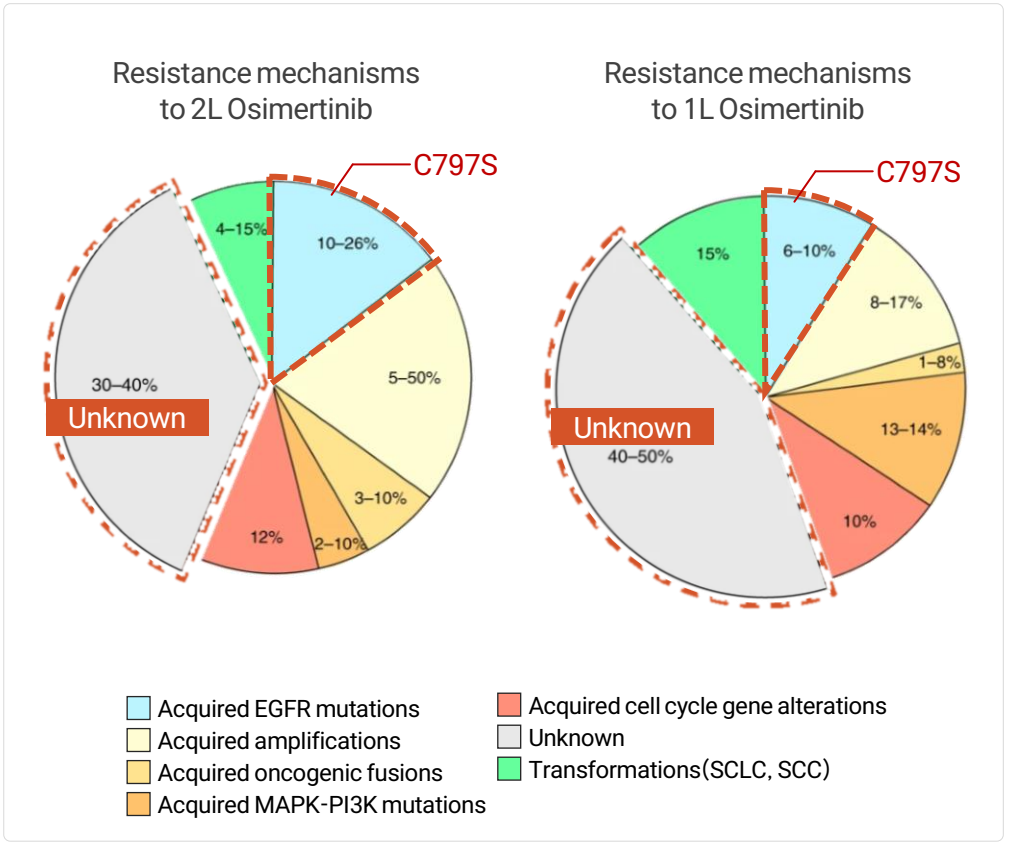
Of Osimertinib resistances, 30~50% are unknown
EGFR del19, L858R, C797S mutations and SOC (including EGFR TKIs) refractory/resistant patients

VRN11. recruiting heavily pre-treated patients



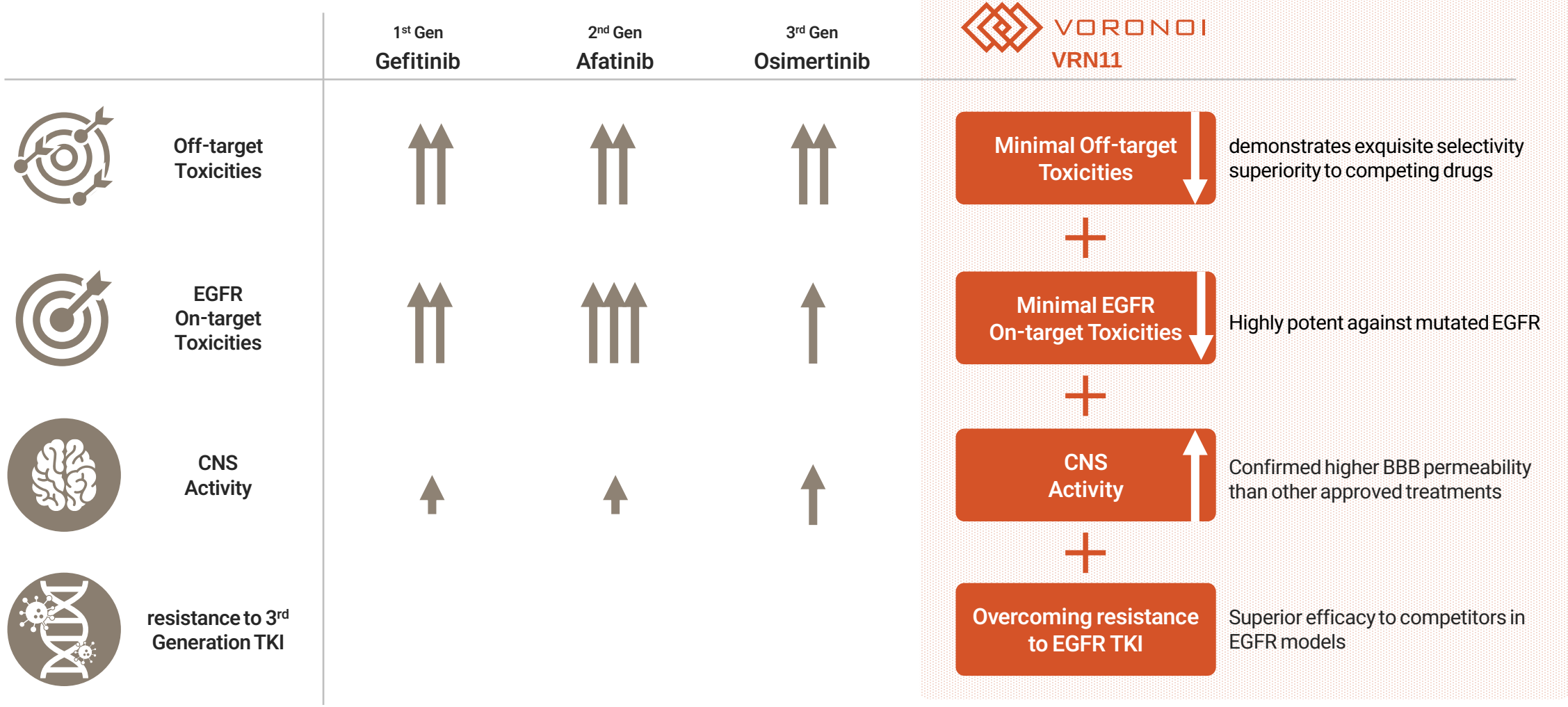
✓ Recruiting patients
who develop brain mets, BCRP/p-gp overexpress or other unknown progression

Resistance mechanisms to Osimertinib in EGFR NSCLC[1]



D:EGFR del19; L:EGFR L858R; G/L/S:EGFR G719X/EGFR L861Q/EGFR S768I; T:EGFR T790M; C:EGFR C797S EGFR: epidermal growth factor receptor; NSCLC: Non-small cell lung cancer; TKI: Tyrosine kinase inhibitor
Source: [1]Leonetti, A. et al. Br J Cancer 121, 725–737 (2019)

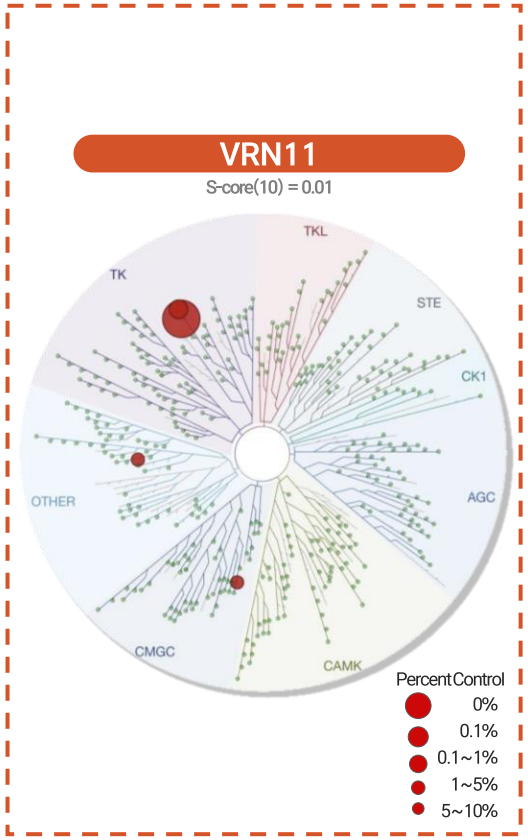
VRN11. Potential First/Best-in-class Profile for EGFR NSCLC

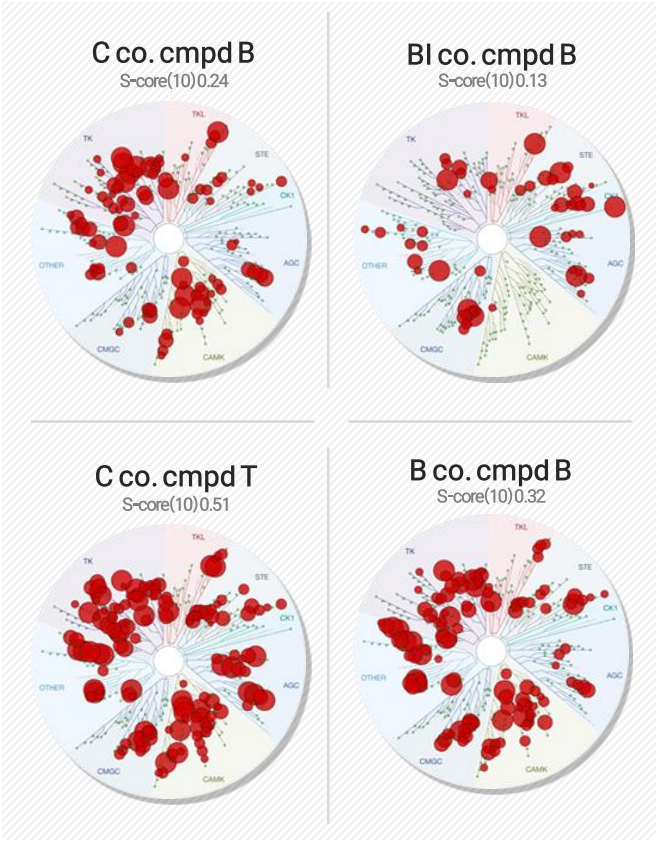


VRN11. Selectivity and Brain Permeability

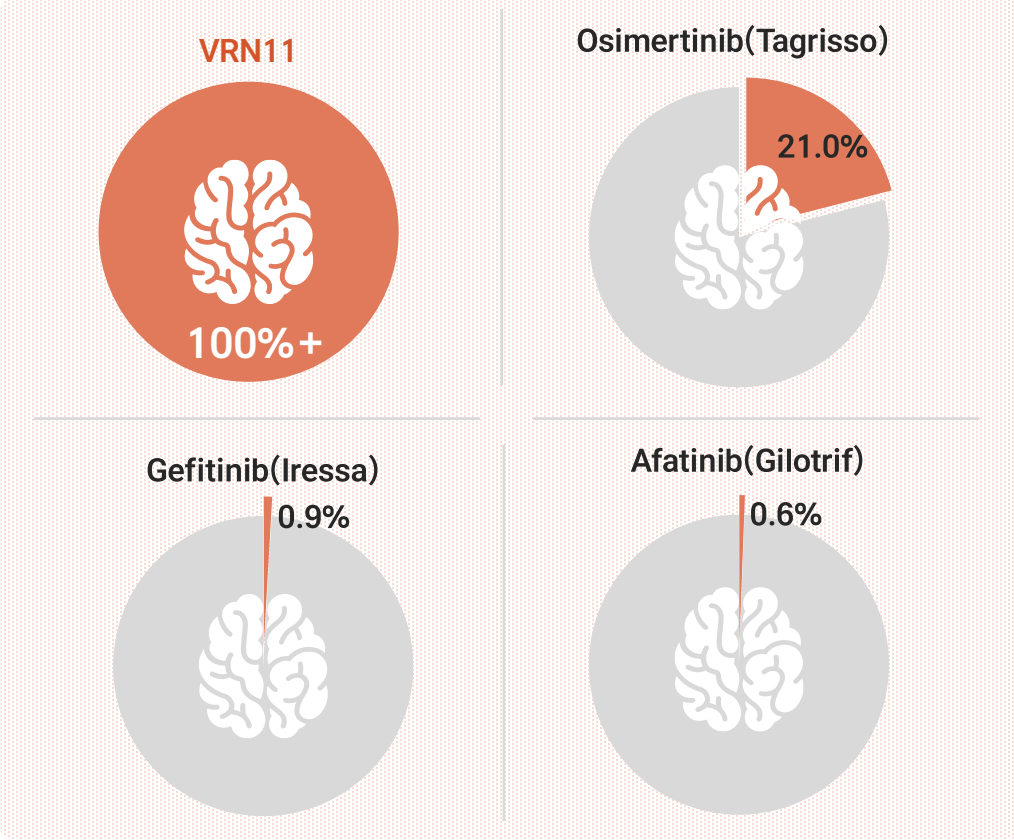
'Selectivity' drives better Safety margin **"Efficacy ↑ Adverse Event ↓"**
High unmet needs for patients with brain metastases **"high brain permeability, high marketability"**

Kinase Selectivity





Brain Permeability (Kp,uu,brain/Rat)[1]

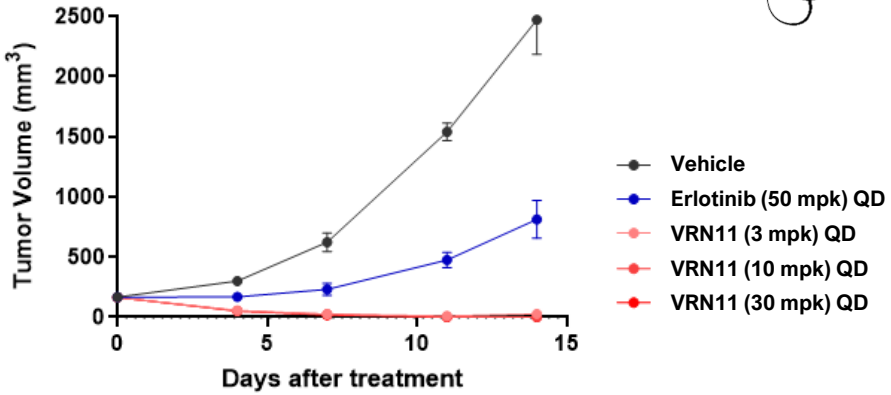


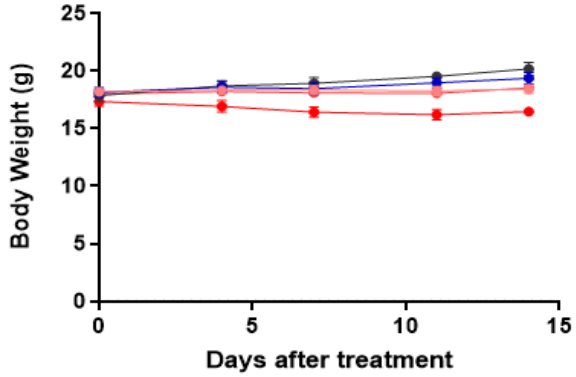
Source: Eurofins DiscoverX Kinomescan, 1 uM concentration, [1]Nicola Colclough et al. Clin Cancer Res 1 January 2021; 27 (1): 189–201

VRN11. *in-vivo* efficacy

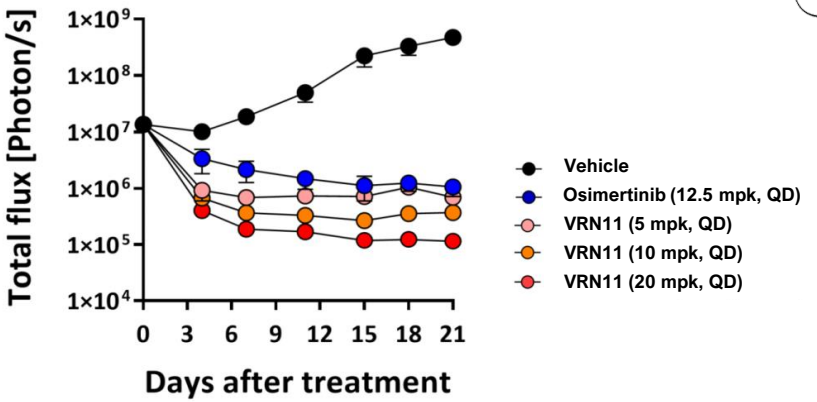
Efficacious in EGFR L858R/C797S as well as EGFR Del19. Also efficacy confirmed in intracranial model

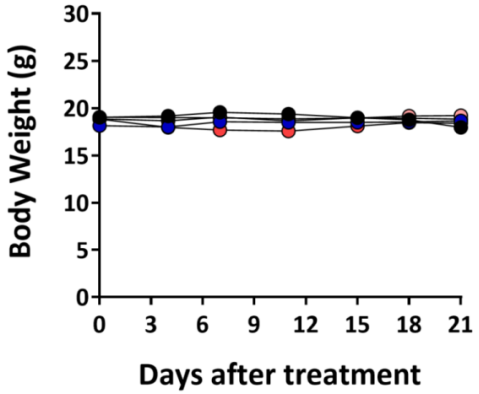
Comparison in subcutaneous model of Ba/F3(EGFR LC)





Comparison in intracranial model of PC9(EGFR del19)

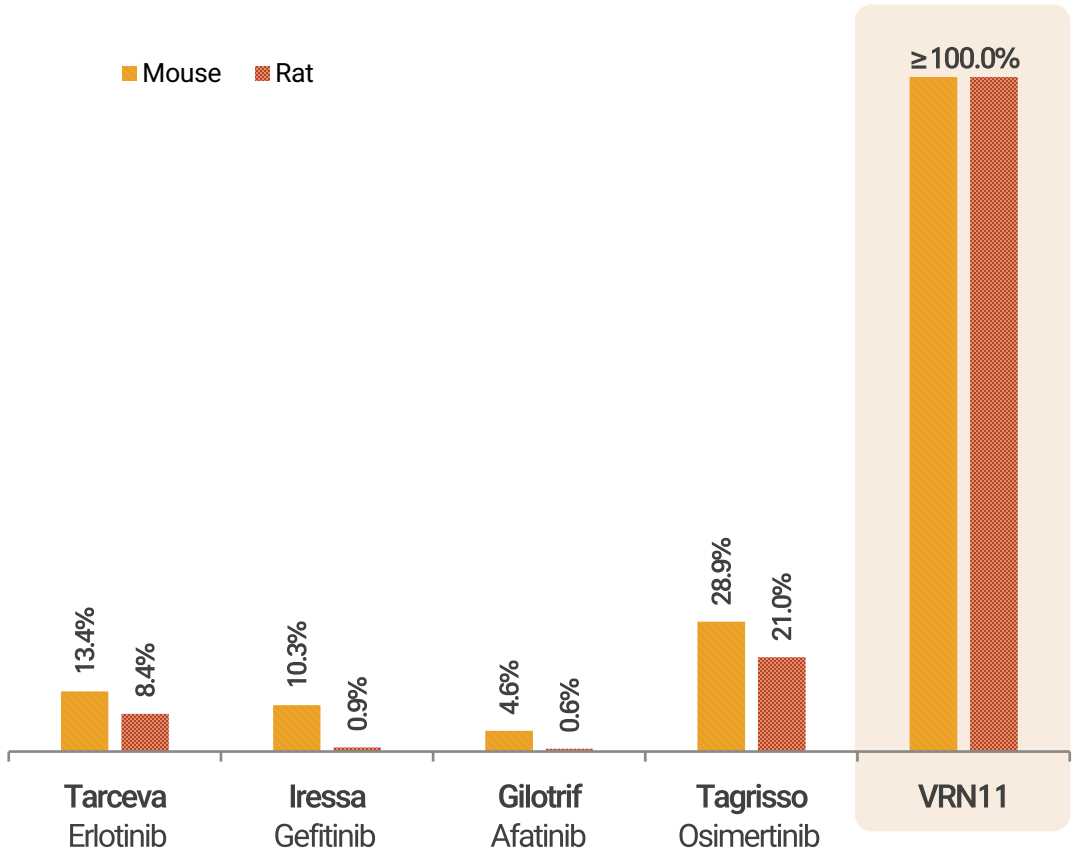




VRN11. Blood-Brain Barrier Permeability of EGFR Targeting Drugs

Confirmed higher BBB permeability than other approved treatments
VRN11 ph.1 trial includes patients with brain metastasis

BBB Permeability of EGFR TKIs (Kp,uu, Brain/ Mouse, Rat)[1,2]



Phase 1 trial of VRN11 includes patients with brain metastases and leptomeningeal metastases

EGFR mutated NSCLC
such as Del19, L858R, C797S, and uncommon mutations
including compound mutations.

+

Include
Brain metastasis(BM),
Leptomeningeal metastasis(LM) patients
- untreated and asymptomatic patients
- treated and controlled* patients

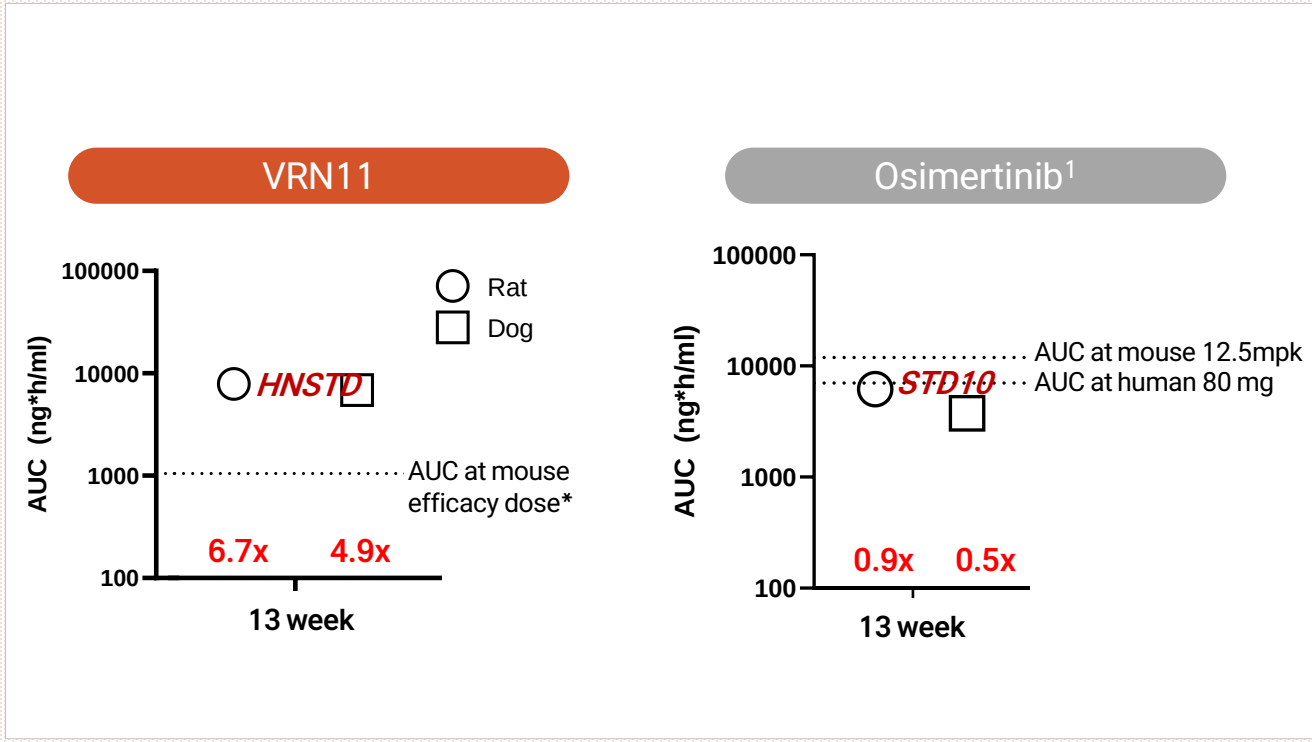
Controlled : Patients with symptoms from brain metastases that can be controlled with steroids up to 10 mg/day.

Source: [1]Nicola Colclough et al. Clin Cancer Res 1 January 2021; 27 (1): 189–201, [2]Drug Metabolism and Disposition April 2019, 47 (4) 393-404

VRN11. Ph1 design reflecting superior safety profile

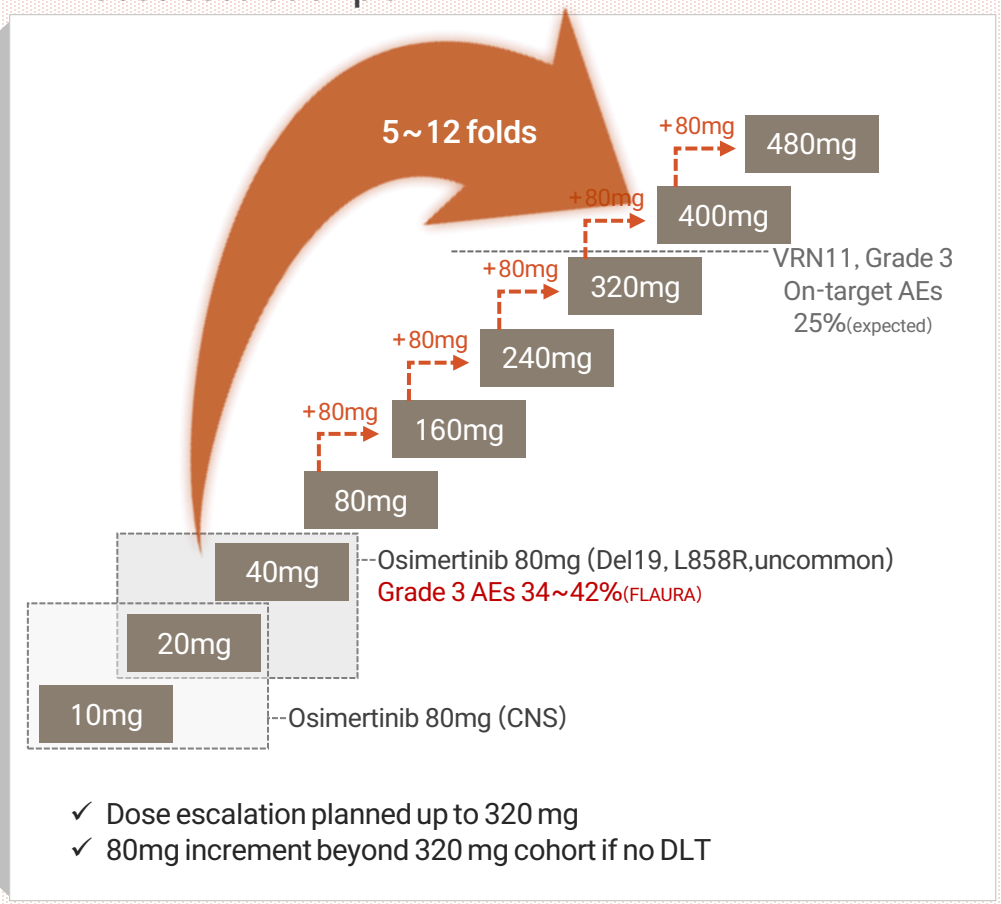
Superior safety margin compared to Osimertinib, enabling x5-10 folds dose escalation without major AEs.
Superior antitumor effect expected from low dose than Osimertinib

Safety Margin



*Mouse efficacy dose: > 90% tumor regression in Del19/C797S models

Ph1 dose escalation plan



✓ Dose escalation planned up to 320 mg
✓ 80mg increment beyond 320 mg cohort if no DLT

Source: [1]FDA review, 13-week GLP tox. studies

VRN11. Phase 1a(Dose escalation) ongoing

Ph1a in progress on SOC resistant/refractory patients
Mostly with Del19, L858R mutation or unknown drivers

Phase 1a Highlights

Key Eligibility

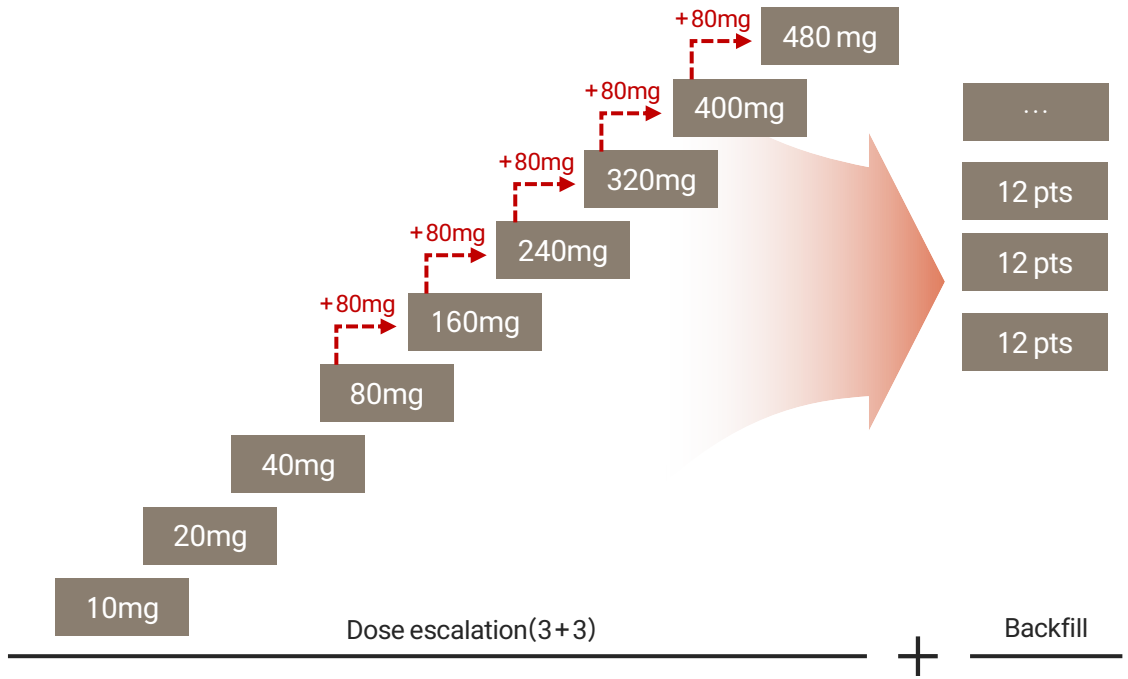
- ✓ EGFR mutated NSCLC such as Del19, L858R, C797S, and uncommon mutations including compound mutations.
- ✓ SOC (including EGFR TKI) resistant/refractory pts
- ✓ Brain metastasis(BM) and Leptomeningeal metasasis(LM) pts (untreated and asymptomatic patients, treated and controlled* patients)

➔ Recruiting & Enrolled Heavily pretreated patients (prior ≥2 lines treatment of EGFR NSCLC)

Clinical Endpoint

- ✓ Primary endpoint: Maximum tolerated dose (MTD), Recommended phase 2 dose (RP2D), Safety and tolerability
- ✓ Secondary endpoint: Overall response rate (RECIST 1.1, RANO-BM) , Duration of response, Pharmacokinetics (PK) and pharmacodynamics (PD)

Dose Escalation, ongoing(up to N ~103)



- ✓ Dose escalation planned up to 320 mg
- ✓ 80mg increment beyond 320 mg cohort if no DLT

VRN11. Unmet needs for SOC (including EGFR TKIs) resistant/refractory patients

Lack of efficacy and safety in EGFR TKI resistant/refractory patients make it difficult to explore 1L settings

SOC resistant/refractory patient trial indirect comparison

	EGFR common mutation(2L+)			
Trial	MARIPOSA2[1]		HERTHENA-Lung01[2]	KEYNOTE-789[3]
Brand name	Chemotherapy	Rybrevant+Chemotherapy	-	Keytruda+Chemotherapy
Drug name	Carboplatin-pemetrexed	Amivantamab +Carboplatin-pemetrexed	Patritumab Deruxtecan	Pembrolizumab +Pemetrexed-platinum
Characteristic	Del19, L858R Osimertinib 1L received 69% Osimertinib 2L received 31%	Del19, L858R Osimertinib 1L received 74% Osimertinib 2L received 26%	Del19, L858R Platinum chemo 100% EGFR TKI 100%	Del19, L858R(T790M 38.8%) EGFR TKI 100%
History of brain metastases	46%	44%	51.1%	28.2%
mPFS (months)	4.2	6.3	5.5	5.6
Adverse events (AEs)	≥Grade3 TEAEs 48% Serious TEAEs 20%	≥Grade3 TEAEs 72% Serious TEAEs 32%	≥Grade3 TEAEs 64.9% (≥Grade4 TEAEs 28.9%)	≥Grade3 TRAEs 43.7% Discontinuation(related Drug) 16.3%

Heavily pretreated patients and EGFR TKI resistant/refractory patients are with high unmet needs

Source: [1]Passaro, A. et al. Annals of Oncology, Volume 35, Issue 1, 77 - 90, [2]Helena A. Yu et al., JCO 41, 5363-5375(2023). [3]James Chih-Hsin Yang et al., JCO 42, 4029-4039(2024).

VRN11. EGFR NSCLC 1L treatment potentials

EGFR NSCLC 1L treatment potentials

VRN11
Ph. 1a heavily pretreated pts (2L+)

- common(D/L) +unknown
- Uncommon(G/L/S) +unknown
- D/L+C797S
- EGFR BM
- EGFR LM

✓ SOC (incl. EGFR TKI) failed patients
✓ Brain mets, BCRP/p-gp overexpressed or other unknown resistant patients

1L settings enrolling naïve patients

- common(D/L)
- uncommon(G/L/S)

Data from heavily treated patients as 2L settings shall enable further exploration to EGFR NSCLC 1L settings

2L to 1L treatment option examples

Osimertinib(EGFR)

2L(AURA) ph.1/2 2013.03~	1L(FLAURA) ph.1/2 2013.03~
Previous treatment with EGFR TKI	Patients must be treatment-naïve

NVL-655(ALK)

2L+(ALKove-1) ph.1/2 2022.06~	1L(ALKAZAR) ph.3; planned 1H2025
Previously-treated ALK+ NSCLC	TKI-naïve ALK+ NSCLC

ORIC-114(EGFR Exon20 insertion)

2L+ ph.1a; 2022.03~	1L ph.1b; planned 2026
Previously-treated EGFR exon20 ins. NSCLC	TKI-naïve EGFR exon20 ins. NSCLC

D:EGFR del19; L:EGFR L858R; G/L/S:EGFR G719X/EGFR L861Q/EGFR S768I; T:EGFR T790M; C:EGFR C797S; BM:Brain metastasis; LM:Leptomeningeal metasasis;

VRN11. EGFR 1L treatment efficacy and safety

EGFR common/uncommon mutation NSCLC naïve patients trial indirect comparison

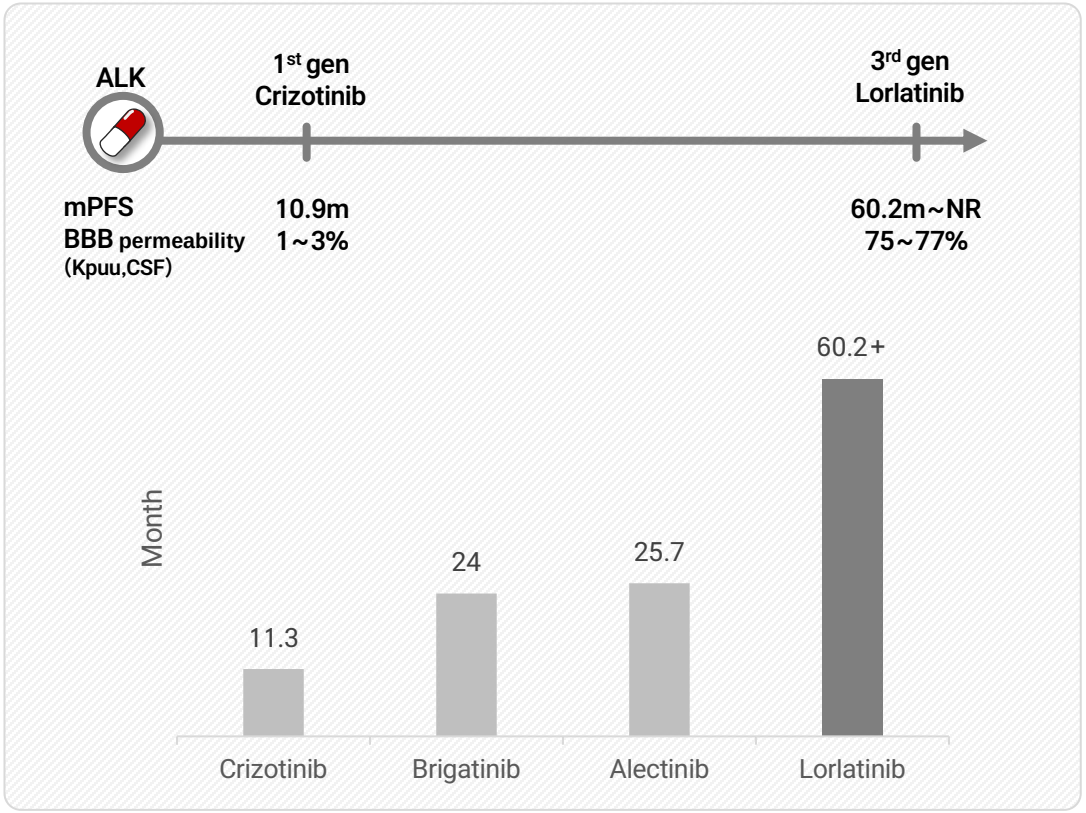
	Uncommon mutation(1L)		Common mutation(1L)			
Trial	LUX-Lung2,3,6[1,2]	KCSG-LU15-09[3]	FLAURA[4]		MARIPOSA[5]	
Brand name	Gilotrif	Tagrisso	Iressa, Tarceva	Tagrisso	Tagrisso	Rybrevant+Lazcluze
Drug name	Afatinib	Osimertinib	Gefitinib, Erlotinib	Osimertinib	Osimertinib	Amivantamab+Lazertinib
Characteristic	Uncommon naïve	Uncommon naïve 61%	Del19, L858R naïve	Del19, L858R naïve	Del19, L858R naïve	Del19, L858R naïve
mPFS (months)	10.7	8.2 (8.2~15.2)	10.2	18.9	16.6	23.7
Adverse events(AEs)	≥Grade3 TRAEs 49% Discontinuations (TRAEs)8%	≥Grade3 AEs 6%(2/36)	≥Grade3 AEs 45%	≥Grade3 AEs 34%	≥Grade3 AEs 43% Serious AEs 33% Discontinuations(TRAEs) 3% Death(AEs) 7%	≥Grade3 AEs 75% Serious AEs 49% Discontinuations(TRAEs) 10% Death(AEs) 8%

VRN11, expecting better efficacy and safety profile than 1L treatment options for EGFR del19, L858R mutations and uncommon mutations

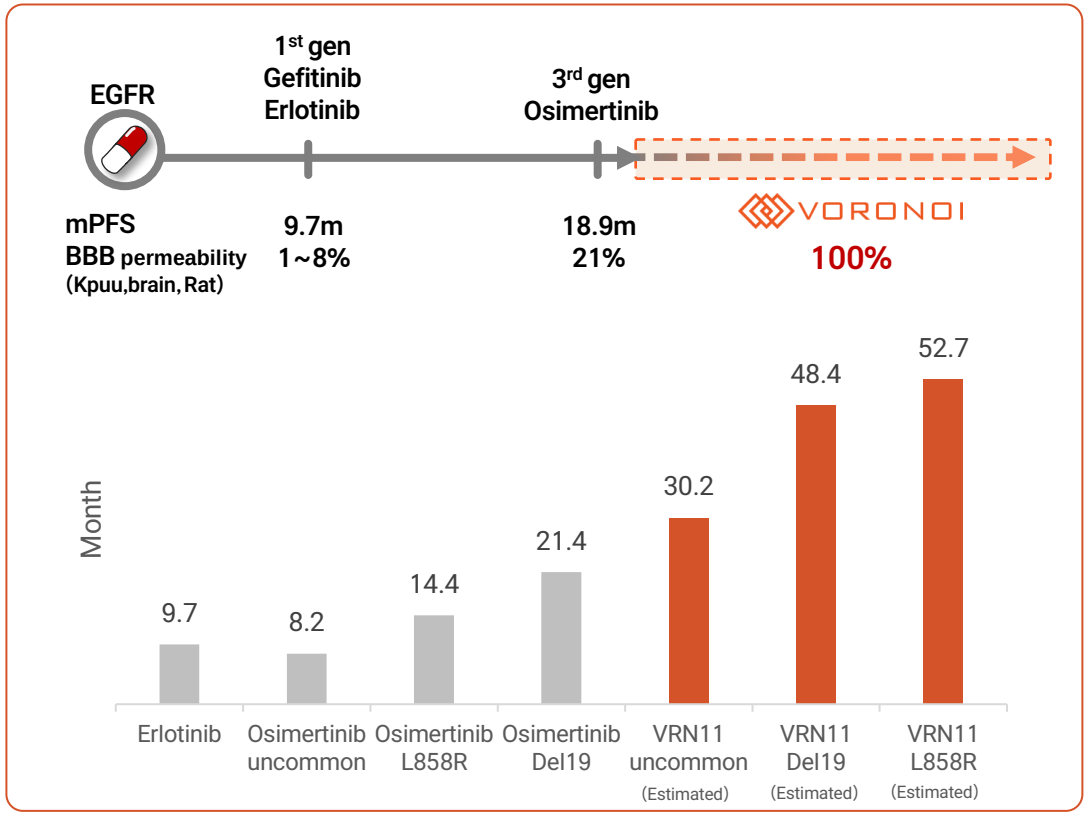
Source: [1]Yang JC, et al., Lancet Oncol. 2015;16(7):830-838. [2]Lecia V. Sequist et al., JCO 31, 3327-3334(2013). [3]Jang Ho Cho et al., JCO 38, 488-495(2020). [4]JC Soria et al., N Engl J Med 2018;378:113-25. [5]ESMO2023

VRN11. Comparison of PFS of targeted therapies

Comparison of PFS of targeted therapies(ALK)

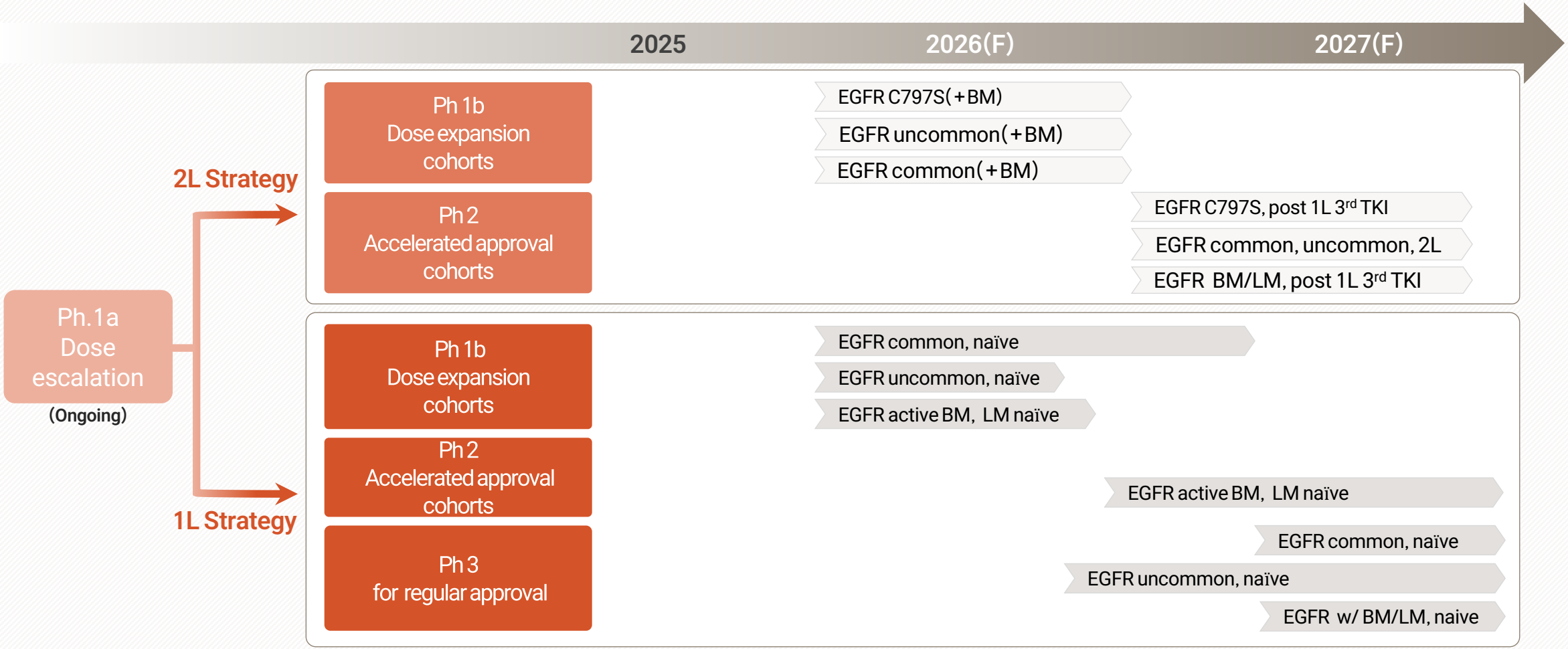


Comparison of PFS of targeted therapies(EGFR)



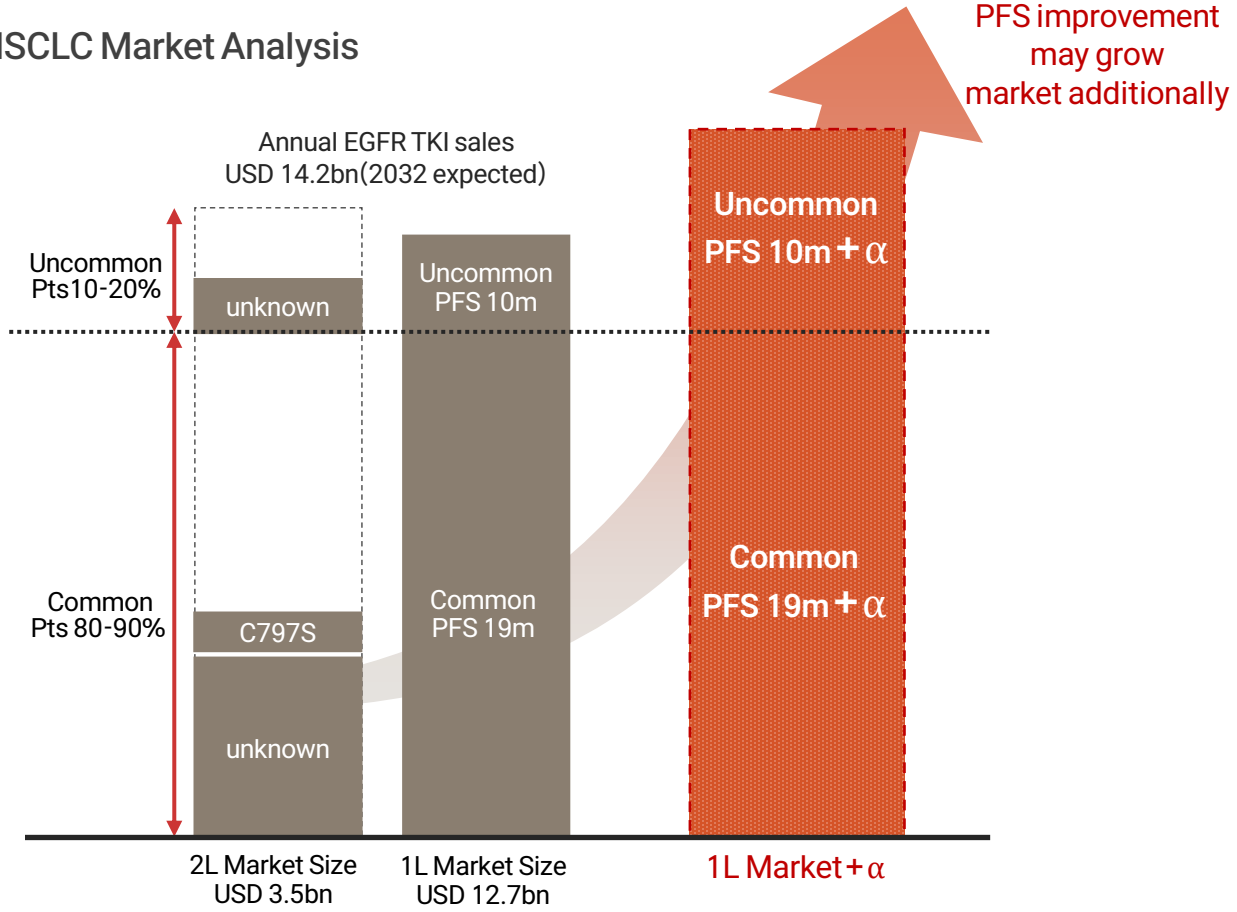
Source: Douillard JY, et al. Br J Cancer 2014;110:55-62, Rosell R, et al. Lancet Oncol 2012;13:239-246, Soria JC, et al. N Engl J Med 2018;378:113-125
Solomon BJ, et al. N Engl J Med 2014;371:2167-2177, Solomon BJ, et al. JCO 0, JCO.24.00581, Toyoaki Hida, Transl Lung Cancer Res. 2023 Aug 30;12(8):1822-1825, Jonathan N. Priantti, et al. JCO 42, 8642-8642(2024), in-house

VRN11. Next planned Steps



VRN11. EGFR NSCLC Market size

EGFR NSCLC Market Analysis



Each EGFR mutation specific differentiation

EGFR Del19, L858R

"Best-in-class Drug"
Exquisite selectivity and brain penetration confirmed
Expecting superior efficacy with good therapeutic margins in clinical settings

EGFR uncommon

"Best-in-class Drug"
Exquisite selectivity and brain penetration confirmed
Expecting superior efficacy with good therapeutic margins in clinical settings

EGFR DC, LC

"First/Best-in class Drug"
No treatment option available
Aiming accelerated approval
with exquisite selectivity profile

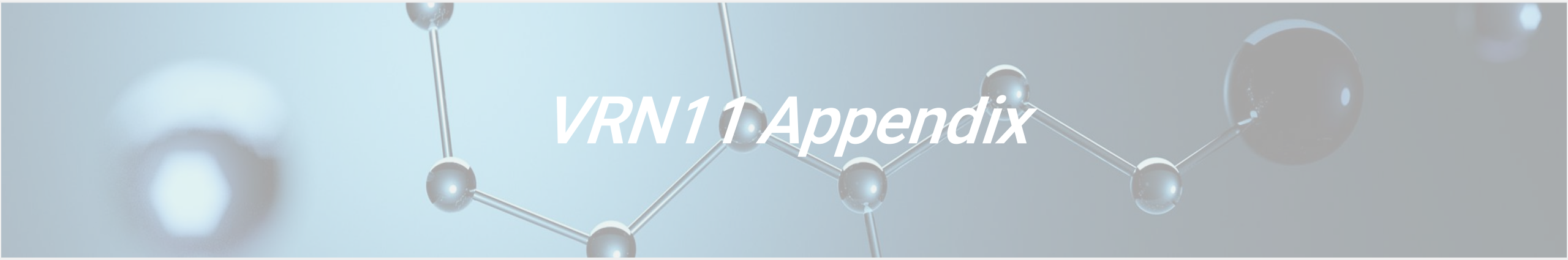
Assumption: 3rd gen EGFR TKIs account for 80% of EGFR common market 80%(*unknown resistance prevalence 40%(1st and 2nd gen TKI, 20%); *C797S resistance prevalence 10%) Unknown resistance prevalence of 50% from EGFR uncommon mutations, 2L treatment PFS assumed x0.6-0.8 of 1L treatment PFS
Source: dataintelo

VRN11. ALK vs EGFR

	Nuvalent	VORONOI
Market Cap (Jan 31, 2025)	**6.1bn USD**	**1.1bn USD**
Addressable Market	**ALK(~3-5% of NSCLC)**	**EGFR(~30-40% of NSCLC)**
	3rd gen, Lorlatinib	4th gen, NVL-655	3rd gen, Osimertinib	4th gen, VRN11*
PFS	NR(64.3 to NR)[1]		Common(D,L) 18.9m Uncommon 9.8m[2]	
Compound mutant Activity[3]	X	O	X	O
Kpuu,brain[3] (rat)	0.1~0.15	0.15~0.2		
Kpuu,brain[4] (mouse)			0.3	1.6
IC-ORR	60%[1]		69%[5]	
Including Untreated/Active BM/LM patients	X	X	X	O
Off-target Toxicities[3]	NO TRK-sparing	TRK-sparing	Major metabolite; off-target related toxicity	Sparing off-targets

*expected

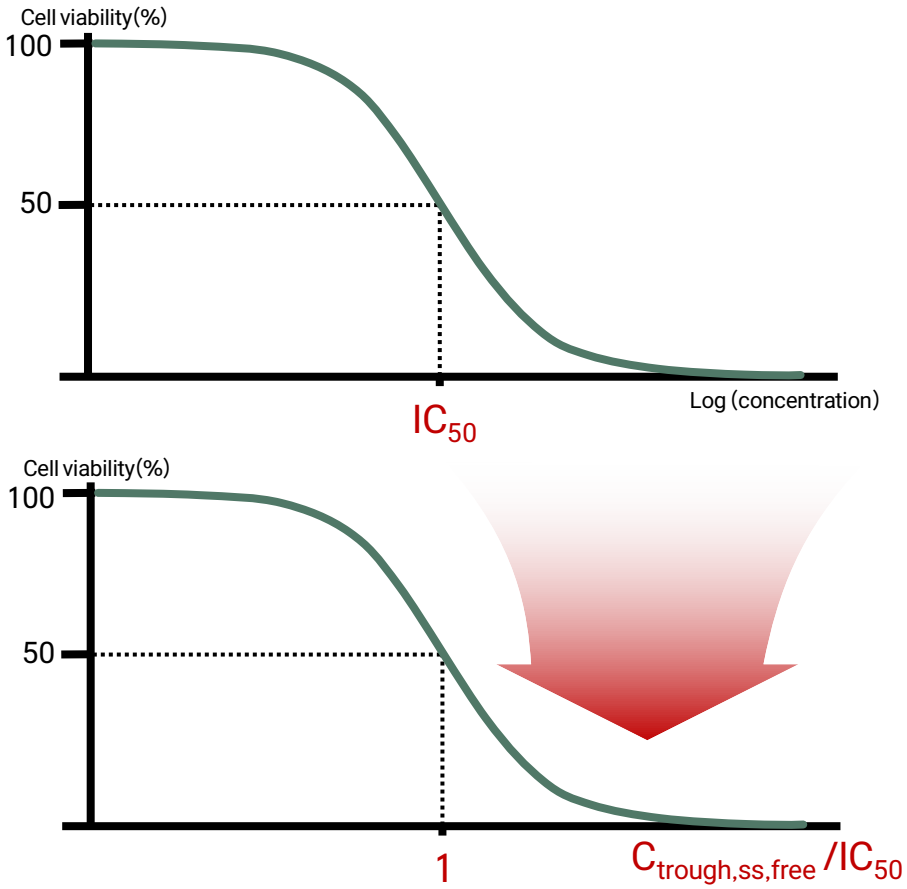
Source: : [1]DOI:10.1200/JCO.24.00581 [2]DOI:10.1001/jamaoncol.2023.5013 [3]Nuvalent Overview(Oct,1,2024) [4]10.1124/dmd.118.084210 [5]DOI: 10.1200/JCO.23.02219
Exchange Rate: 2025.01 average 1 USD = 1455.79 KRW



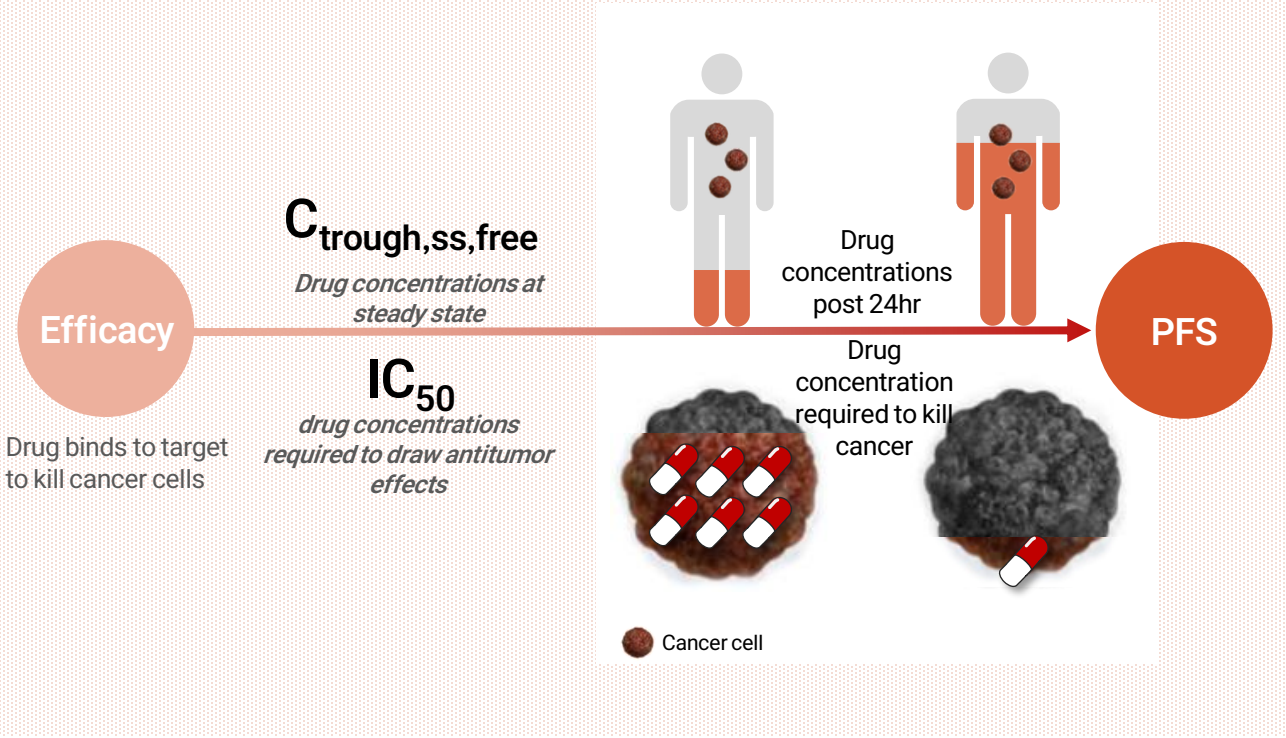
VRN11 Appendix

Reinterpretation of IC_{50} data

PK drives antitumor effects



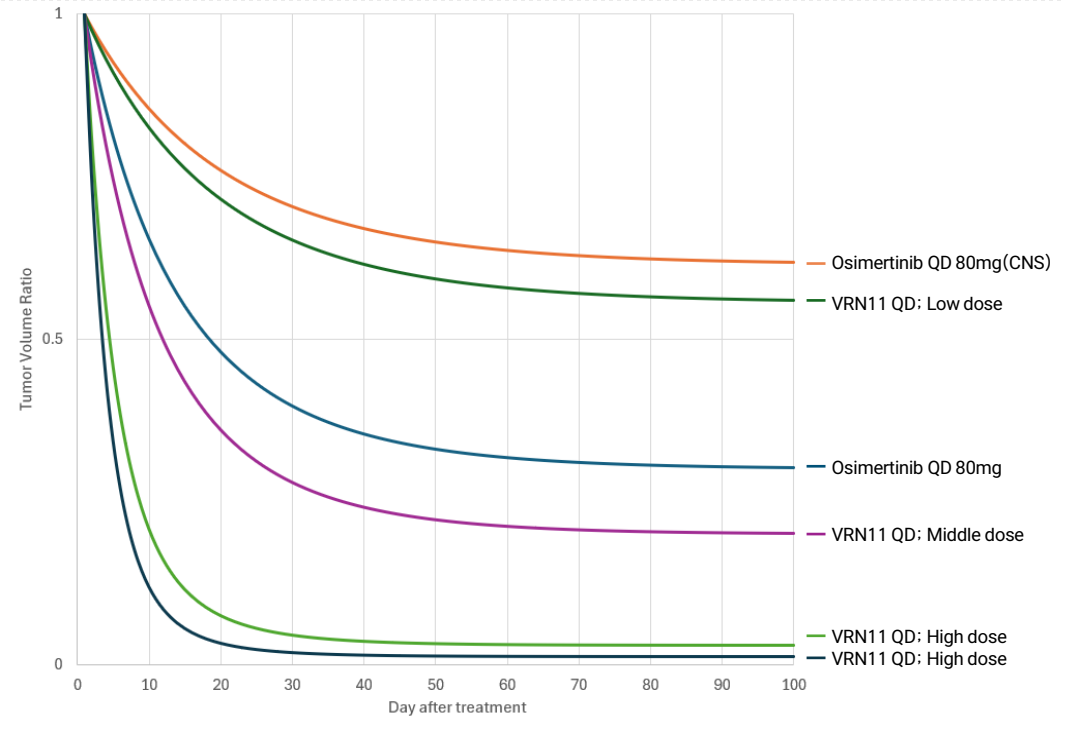
Pharmacokinetics (PK) and antitumor effect



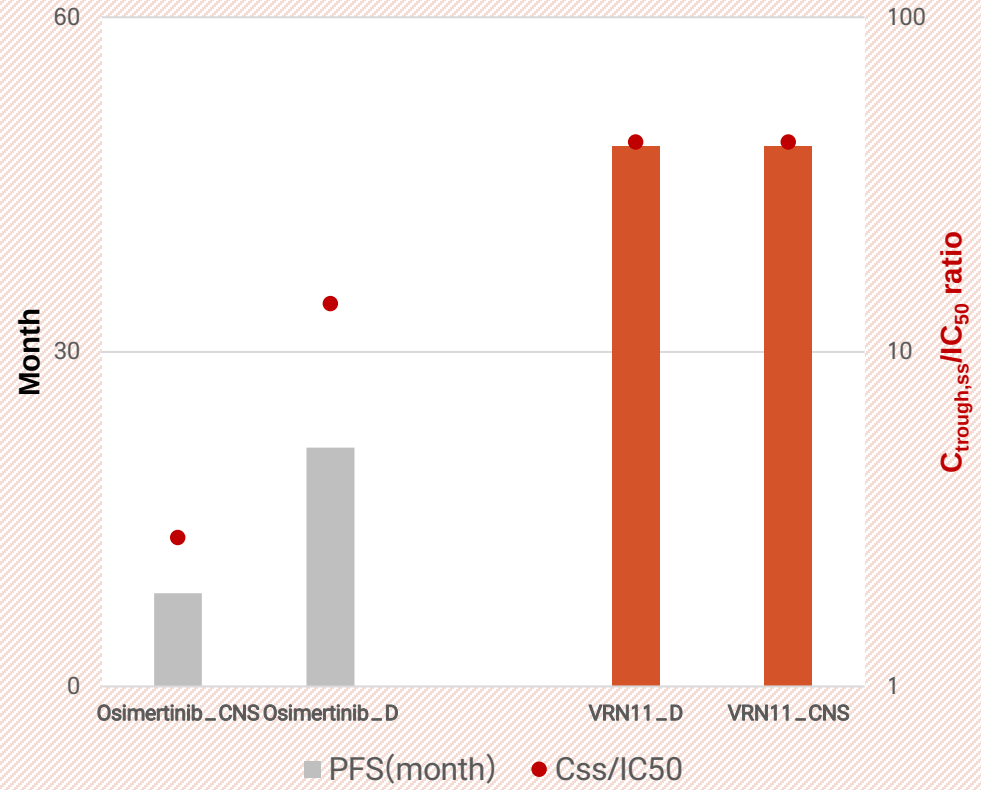
Simulation of cancer cure rate, PFS(EGFR Del19)

Persister cancer cells lead to bypass or acquired resistance mechanism, resulting in shorter mPFS

C_{trough}/IC_{50} - Cancer cure rate relationship

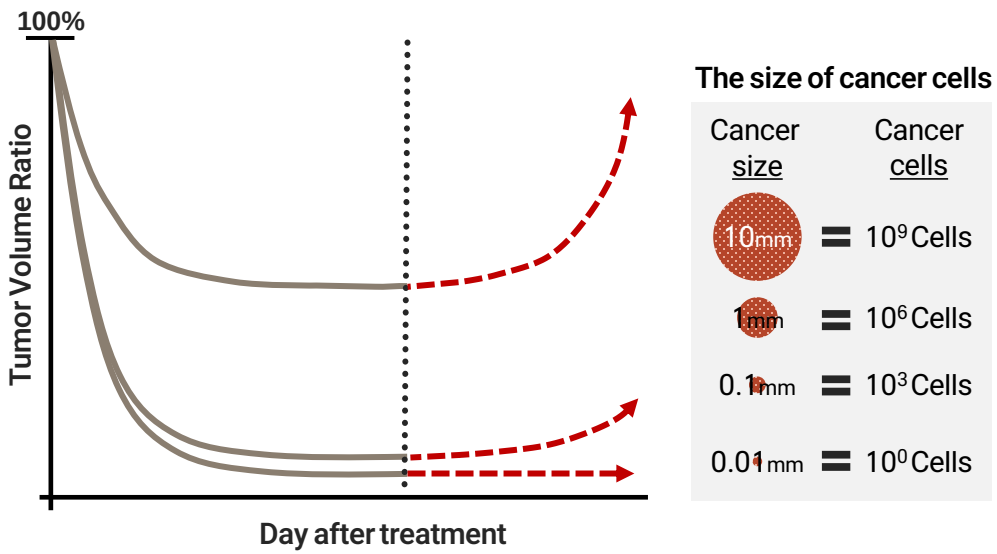


C_{trough}/IC_{50} - PFS relationship

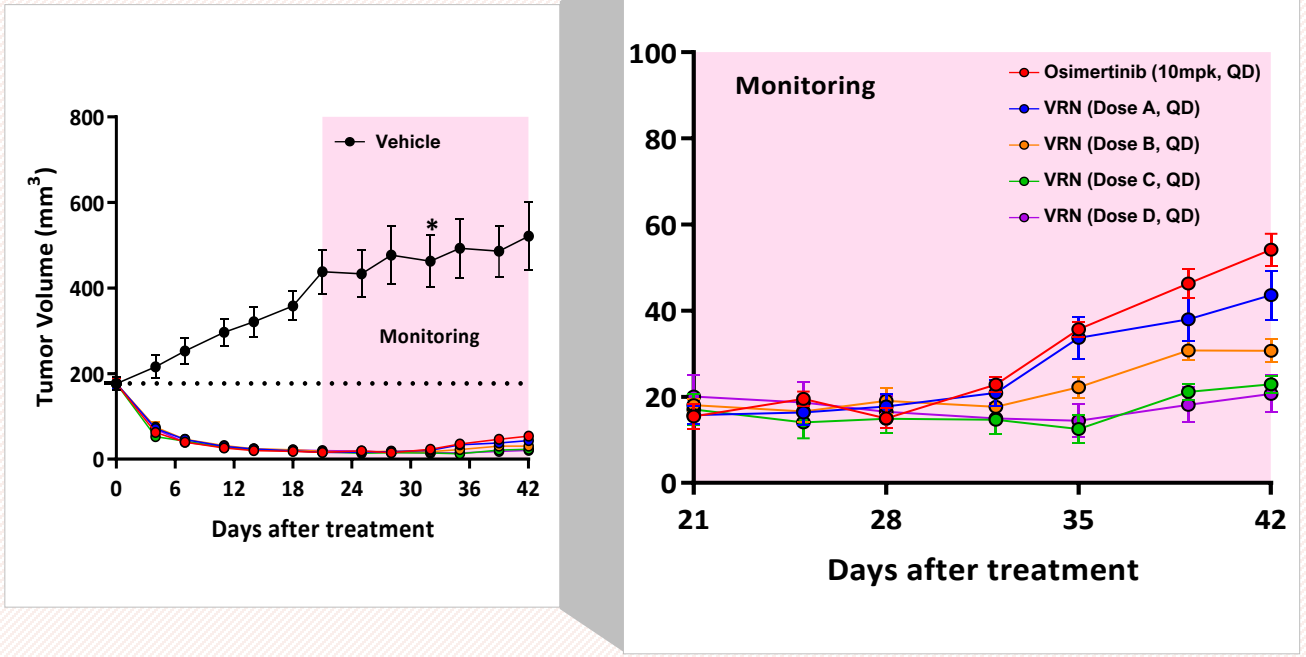


Persister Cancer Cell, Treatment Resistance and PFS

Simulation of cancer cure rate

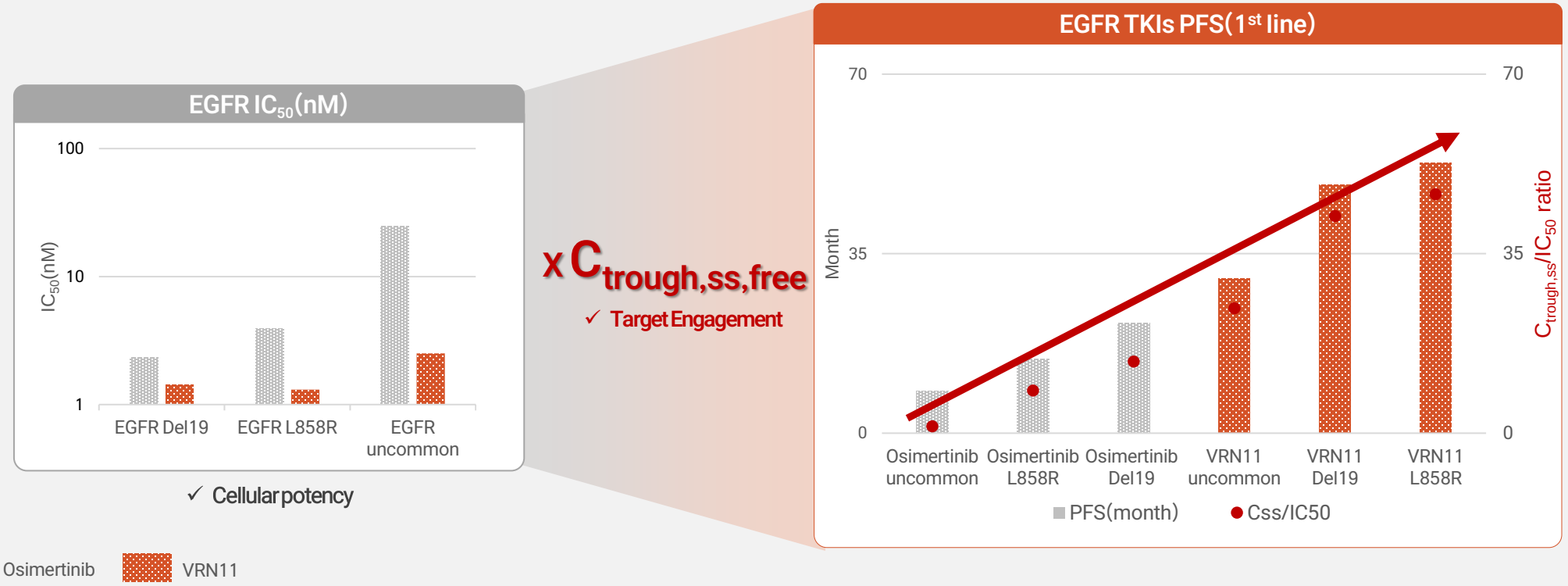


EGFR L858 CDX SC model



C_{trough}/IC_{50}- mPFS relationship (EGFR)

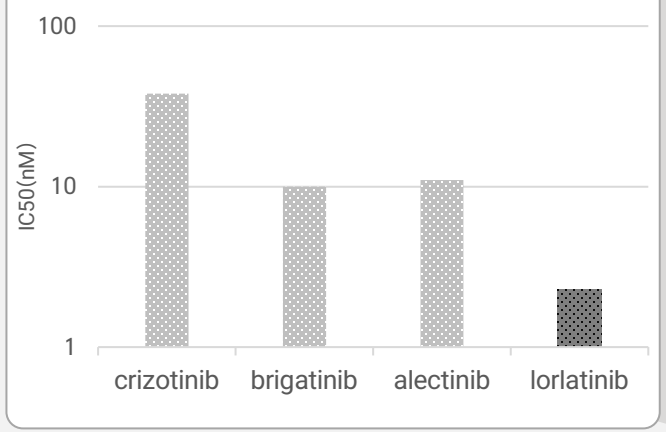
NSCLC EGFR case



C_{trough}/IC_{50}- mPFS relationship (ALK)

NSCLC ALK case

ALK fusion IC_{50}(nM)

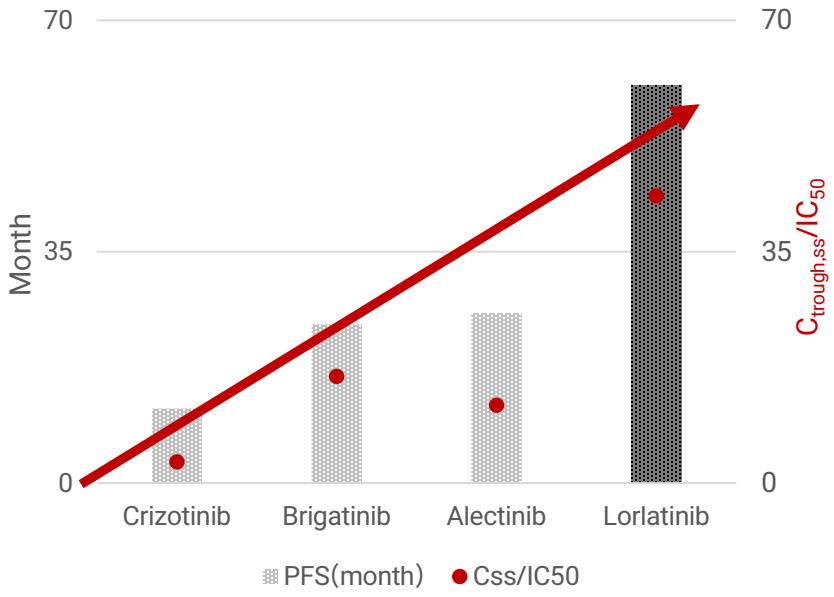


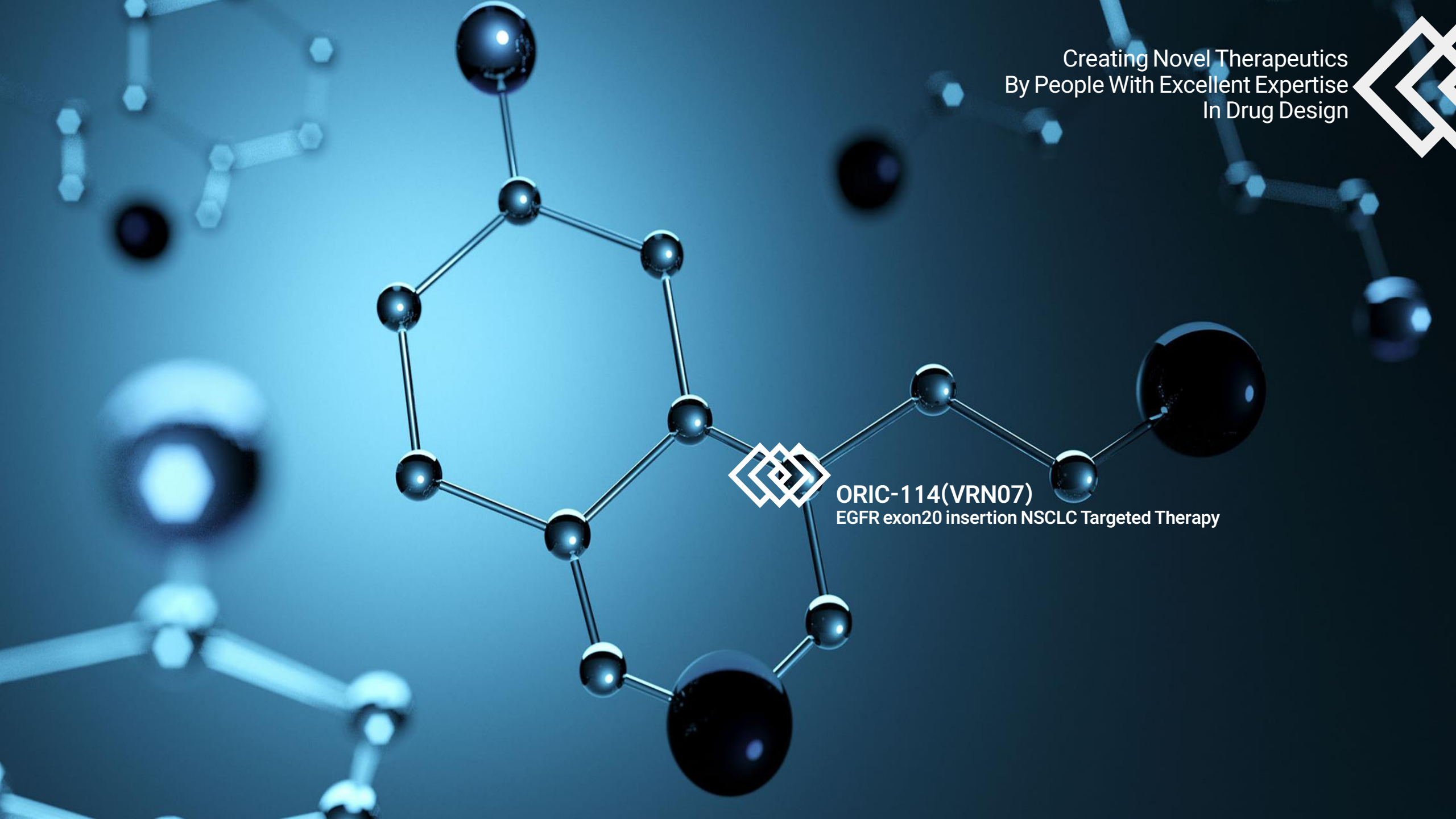
✓ Cellular potency against ALK mt

x $C_{trough,ss,free}$

✓ Target Engagement

ALK TKIs PFS(1st line)




Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design
ORIC-114(VRN07)
EGFR exon20 insertion NSCLC Targeted Therapy

VRN07(ORIC-114). aiming 1st/2nd line Approval for EGFR Exon20 Ins. NSCLC

VRN07(ORIC-114) aiming Second-line Approval for EGFR Exon20 Ins. NSCLC

1. **Complete Response(CR)** in heavily treated patients
2. 2L setting potential for Amivantamab failed/resistant patients
3. **Brain activity in active Brain Metastasis patients**
4. **No grade 3+ off-target toxicity** reported yet

VRN07(ORIC-114). EGFR exon20 inhibitor Competitive Landscape

ORIC-114 is the only EGFR exon 20 inhibitor to demonstrate a confirmed complete systemic response and confirmed complete CNS response

- EGFR exon 20 inhibitor clinical studies typically EXCLUDE:
  - Prior EGFR exon 20 treatment
  - Untreated CNS metastases
- ORIC-114 trial enrolled significantly higher percentage of patients with prior EGFR exon 20 treatment and baseline CNS metastases
- Despite more challenging patients, ORIC-114 demonstrated:
  - Systemic complete response
  - CNS complete response in untreated CNS metastases
  - Responses post-amivantamab

	Amivantamab	CLN-081	Sunvozertinib	Furmonertinib	BLU-451	ORIC-114
Trial	Phase 1	Phase 1	Phase 2	Phase 1	Phase 1	Phase 1
ENROLLMENT						
Prior EGFR ex20i Allowed (1)	No	No	No	No	Yes	**Yes**
% Prior EGFR ex20i	1%	4%	3%	NR	75%	**81%**
Untreated CNS Mets Allowed	No	No	No	No	Yes	**Yes**
% Baseline CNS Mets	22%	38%	32%	34%	58%	**86%**
CLINICAL ACTIVITY						
Systemic Complete Response	Yes	No	No	No	No	**Yes**
CNS Complete Response in Untreated CNS Mets (2)	No	No	No	No	No	**Yes**
ORR in EGFR ex20i Naive	~40%	~41%	~61%	42%	TBD	**TBD**
Post-Amivantamab Response	NA	No	Yes	No	No	**33% confirmed ORR (at 75 mg)**

Source: ORIC company overview January 2025

VRN07(ORIC-114). First Clinical Evidence of Efficacy in Patients with Active Brain Metastasis

Active brain metastases – Unprecedented among EGFR targeted therapies

Limitations of exciting EGFR targeted therapy

Patient Selection

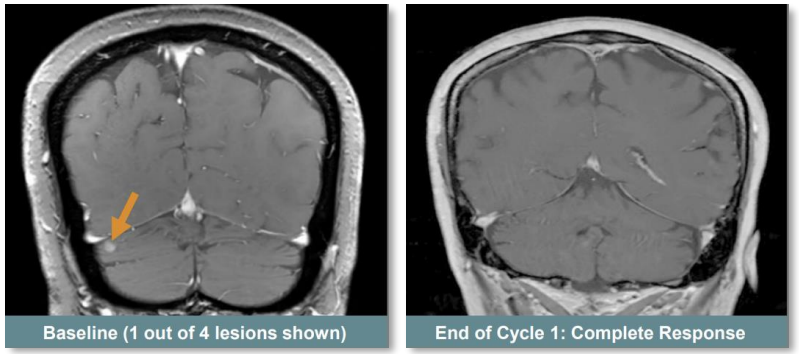
Key inclusion criteria included presence on tissue biopsy of ≥1 of the two common *EGFR* mutations associated with TKI sensitivity (ex19del, L858R) and treatment-naïve for locally advanced or metastatic NSCLC. Key exclusion criteria included symptomatic and unstable brain metastases (patients with asymptomatic and stable brain metastases were eligible if radiation therapy or surgery was completed and no steroids were received for >2 weeks before random assignment).

VRN07(ORIC-114). Patient Population

- Any advanced solid tumor with locally documented:
  - EGFR exon 20 insertion mutation
  - HER2 exon 20 insertion mutation
  - HER2 amplification or overexpression
  - Atypical EGFR mutation (NSCLC only)
- Prior chemotherapy
- All other prior therapies allowed, including prior exon 20 targeted therapies
- RECIST v1.1 measurable disease
- Patients with CNS metastases allowed, including asymptomatic untreated CNS metastases
- ECOG 0-1 → **Active brain metastatic patients are allowed**

VRN07(ORIC-114). the first case of CR observed in patient with active BM

	BM(%)
VRN07 (ORIC-114)	86 (including active BM)
Amivantamab	22
Mobocertinib	35
Furmonertinib	29
Sunvozertinib	32
BLU-451	58 (discontinued)
Zipalertinib	38



- **CNS metastases at baseline:** Four active CNS non-target lesions
  - Previously untreated
  - No prior surgery
  - No prior radiation
- **CNS response:** Complete response after Cycle 1 (**100% reduction of all 4 CNS lesions**), confirmed after Cycle 2

8 out of 13 brain metastatic patients responded

✓ **One patient showed CR**

✓ **Seven patients showed PR / SD**

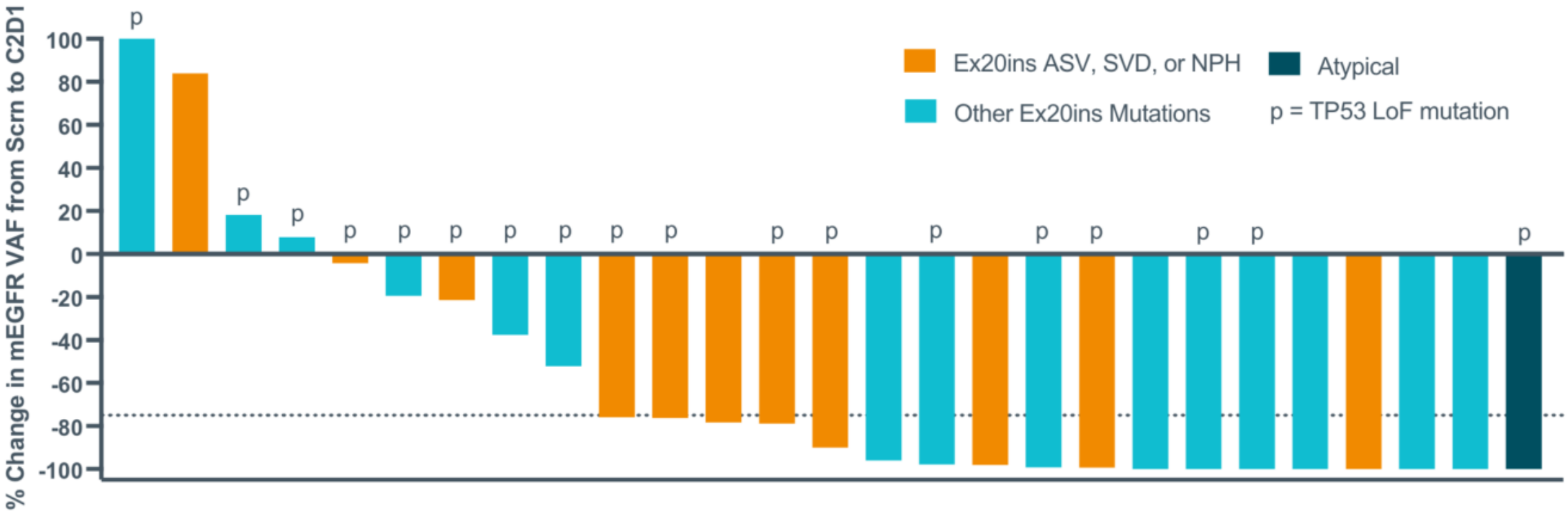
The first clinical case demonstrating CR in active BM

Source: DOI: 10.1200/JCO.23.00515 Journal of Clinical Oncology 41, no. 26 (September 10, 2023) 4208-4217., AACR2022, ESMO2023

BM: Brain metastasis; CNS: Central nervous system; CR: Complete response EGFR: epidermal growth factor receptor; HER2: Human Epidermal Growth Factor Receptor 2; PD: Partial response; NSCLC: Non-small cell lung cancer; SD: Stable disease; TKI: Tyrosine kinase inhibitor

VRN07(ORIC-114). Molecular Response in NSCLC patients

Ph.1b , ctDNA



ORIC-114 achieved >75% molecular depletion in mutant EGFR by week 4 in 67%(18/27)

Source: ENA2024

VRN07(ORIC-114). First-line Treatment Potential

Initiation of expansion cohorts for treatment-naïve patients (2024.04)

ORIC

ORIC Pharmaceuticals Announces First Patients Dosed Across Three Expansion Cohorts in Phase 1b Trial of ORIC-114 in Patients with Mutated NSCLC

April 15, 2024 at 4:15 PM EDT

Additionally, the company initiated an extension cohort to evaluate ORIC-114 for the treatment of patients with first-line, treatment-naïve EGFR exon 20 NSCLC

Expect to report updated Phase 1b data in the first half of 2025

Phase 1 update (2024.05)

- ph1/2 patients in total
  280 pts → 350 pts
- # of clinical sites
  26 sites → 34 sites
- US, AU, KR + additional countries
  UK/Canada/Poland/Taiwan/HK

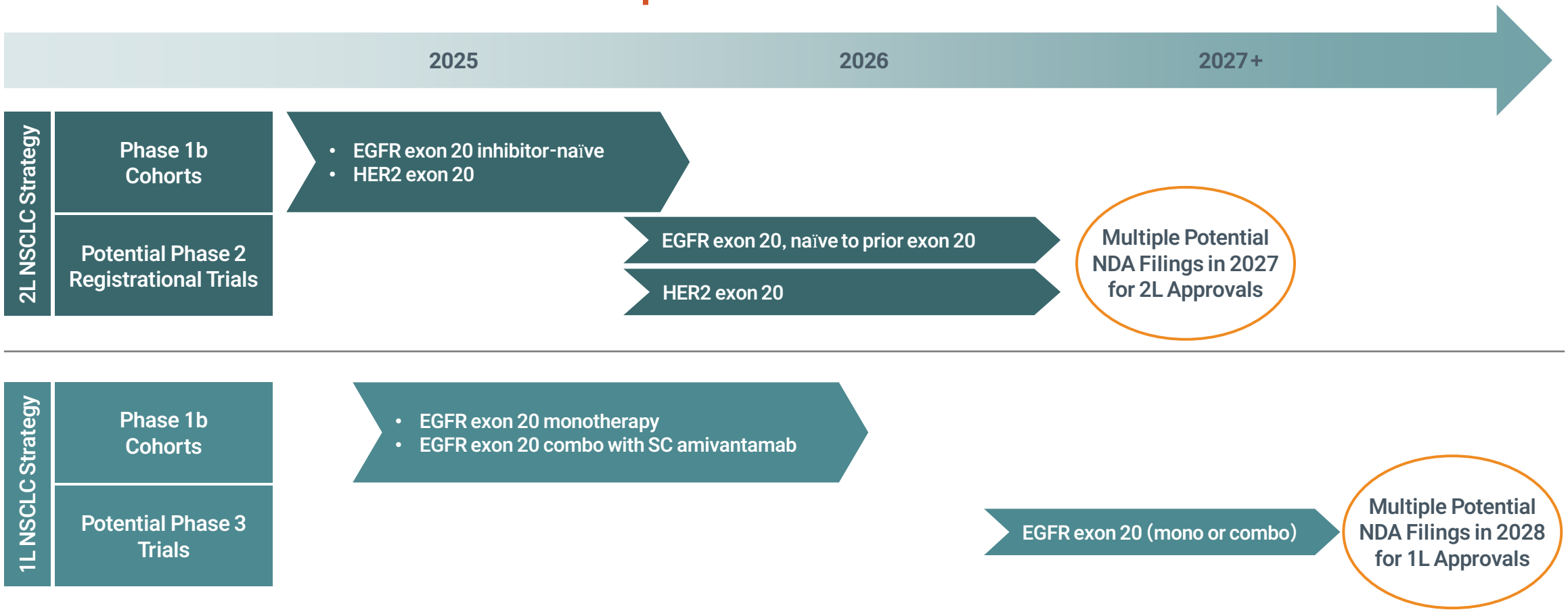
Clinical Collaboration with Johnson & Johnson(2025.01)

ORIC Johnson&Johnson

Collaboration Overview	• ORIC-114 plus SC amivantamab to be evaluated in 1L NSCLC with EGFR exon 20 insertions. • ORIC retains development and commercialization rights to ORIC-114
Combination Rationale	• Potential for deeper and more durable clinical activity than either agent alone → ORIC-114 provides CNS exposure to treat and/or prevent brain metastases → Amivantamab provides activity against potential TKI resistance mechanisms

Source: ORIC company overview January 2025

VRN07(ORIC-114). Planned Next Steps and Potential Registrational Path(s) in EGFR exon20 insertion NSCLC patients



Updated Phase 1b data expected in 1H 2025 with the potential initiation of multiple accelerated registrational cohorts expected in 2H 2025; potential for ORIC-114 1L registrational trial(s) initiation in 2026

Source: ORIC company overview January 2025

VRN07(ORIC-114). EGFR exon20 insertion. 1st/ 2nd treatment

EGFR exon20 insertion NSCLC trials indirect comparison

	EGFR exon20 insertion(1L)		EGFR exon20 insertion(2L)		
Trial	PAPILLON[1]	FAVOUR[2]	CHRYSALIS[3]	WU-KONG6[4]	FAVOUR[2]
Brand name	Rybrevant+Chemotherapy	-	Rybrevant	-	-
Drug name	Amivantamab +Carboplatin-pemetrexed	Firmonertinib	Amivantamab	Sunvozertinib	Firmonertinib
Characteristic	No previous treatment	Treatment naïve	previous chemotherapy	Received 1-3 line of prior treatment	Previously treated
Brain metastases (%)*	23%	17%	22.2%	32%	29%
mPFS (months)	11.4	-	8.3	-	-
Adverse events(AEs)	≥Grade3 AEs 75%	≥Grade3 TRAEs 13% Serious TRAEs 3%	≥Grade3 AEs 35%	≥Grade3 off-target AEs(Blood CPK increase 17.3%, Anema 5.8%)	≥Grade3 TRAEs 29% Serious TRAEs 18%

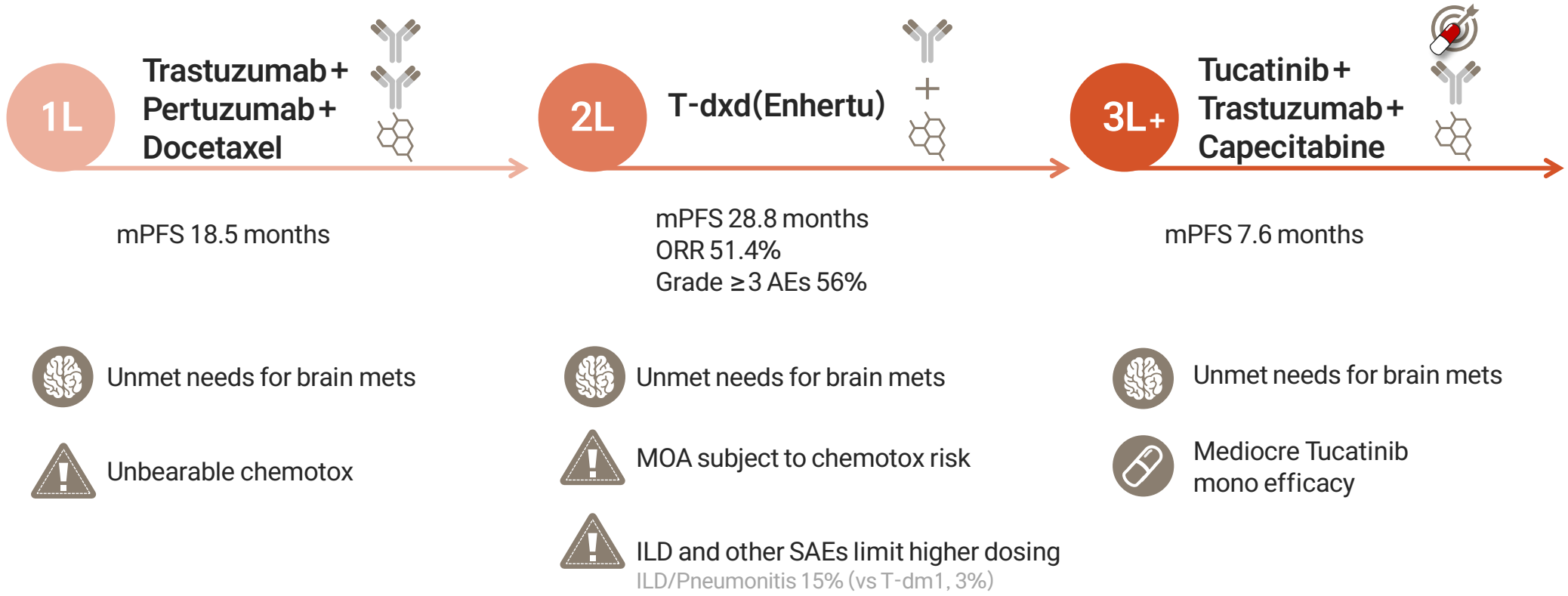
*History or presence of brain metastases

Source: [1]Zhou C, et al. N Engl J Med. 2023;389(22):2039-2051. [2]IASLC2023 [3]Park K, et al. J Clin Oncol. 2021;39(30):3391-3402. [4]ASCO2023


Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design
VRN10. HER2+
Breast Cancer Targeted Therapy

VRN10. HER2 positive Breast Cancer Treatment Guideline

VRN10 to overcome limitations of existing treatment options



Source: Baselga J, et al. N Engl J Med. 2012;366(2):109-119., Hurvitz, Sara A et al. The Lancet, Volume 401, Issue 10371, 105 – 117, Murthy RK, Loi S, et al.N Engl J Med 2020;382:597-609.
AEs: adverse events, ILD: interstitial lung disease

VRN10. HER2 positive Breast Cancer Treatment Guideline (Expected)

1L SOC Enhertu shifts treatment paradigm
Yet VRN10 may be able to address several opportunities

Standard of Care

1L T-dxd(Enhertu)

Results of Clinical trial

Destiny-Breast09 trial
Data readout 2025

Key Limitations

- Unmet needs for brain mets
- MOA subject to chemotoxic agents
- ILD and other SAEs limit higher dosing

1L+ What is Standard of care after 1st line treatment?

✓ post-Enhertu potentials

Unmet needs for brain mets
➔VRN10,
10x brain permeable than Tucatinib

✓ ADC combo potentials

ILD and other SAEs limit higher dosing
➔ Covalent inhibitor VRN10 and HER2 ADC Enhertu combo expects synergy

AEs: adverse events, ILD: interstitial lung disease

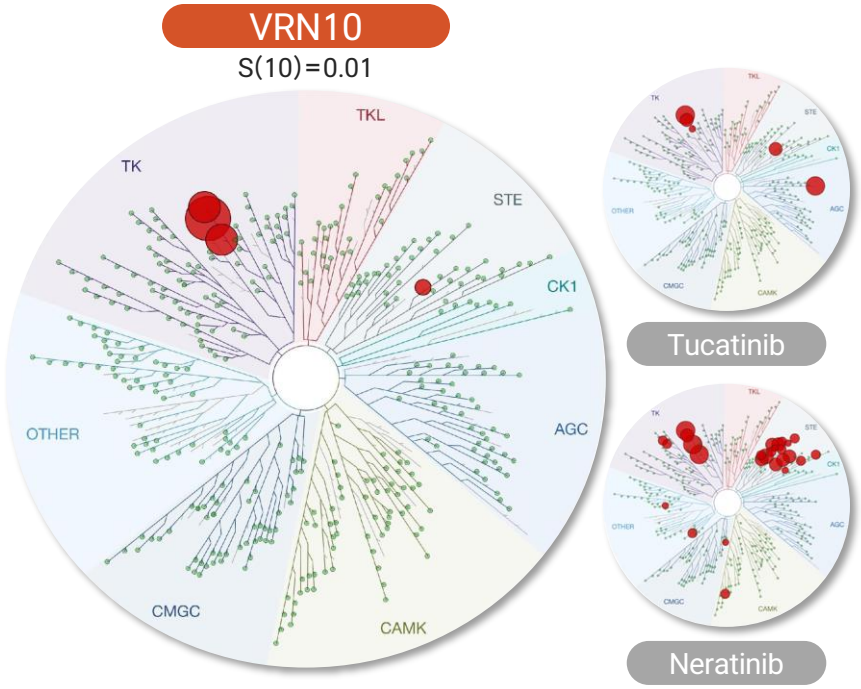
VRN10. HER2 positive TKI. Competitive Landscape

	VORONOI VRN10	Boehringer Ingelheim Zongertinib	Puma Biotechnology Neratinib	Roche ZN-A-1041	Pfizer Tucatinib
HER2 selectivity over EGFR	+++	+++	-	+	+++
Potency to resistant mutants	+++		+++	+	+
Intracranial efficacy	+++	-	-	+++	+
Binding mode	**Covalent**	Covalent	Covalent	Non-covalent	Non-covalent
GSH reactivity	**Low**	Moderate	High		Low
HER2 ADC Internalization	**Promote**		Promote	No promote	No promote
BCRP substrate	**No**	Yes	No		Yes

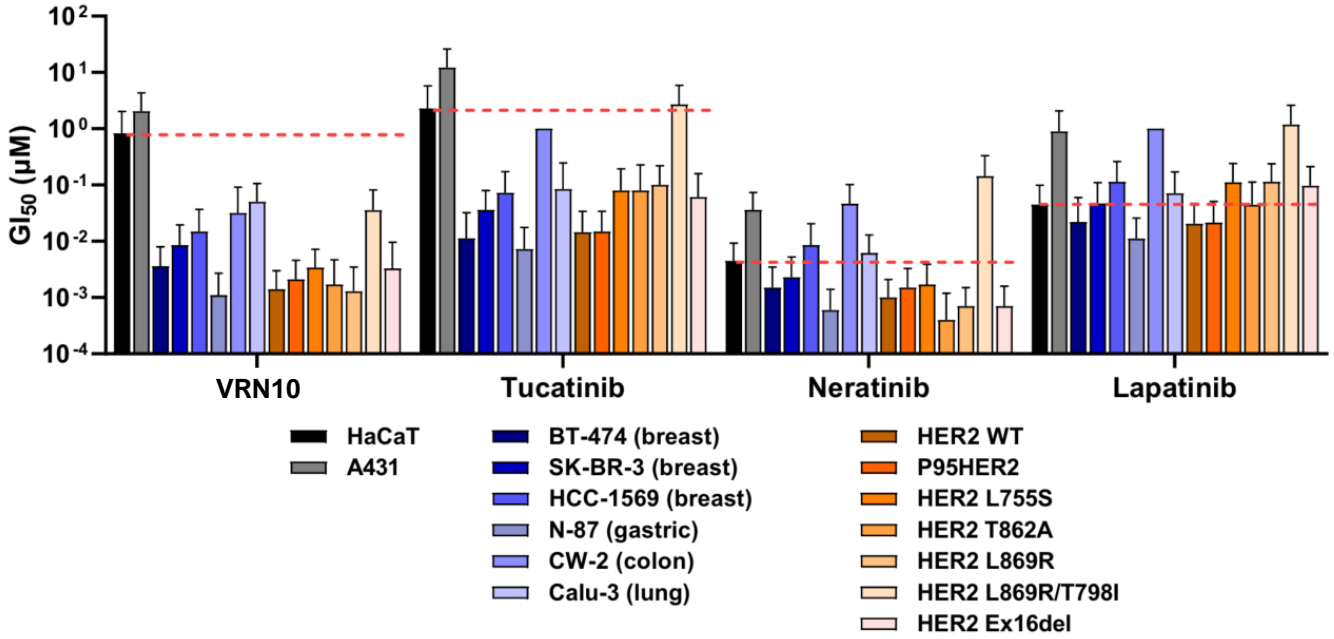
VRN10. Preclinical *in-vitro* : Selectivity

Exquisite selectivity over EGFR(HER1), expecting lower diarrhea and skin rash than approved HER2 drugs

Highly selective & potent to HER2



Potent HER2 inhibitor with wider selectivity over EGFR

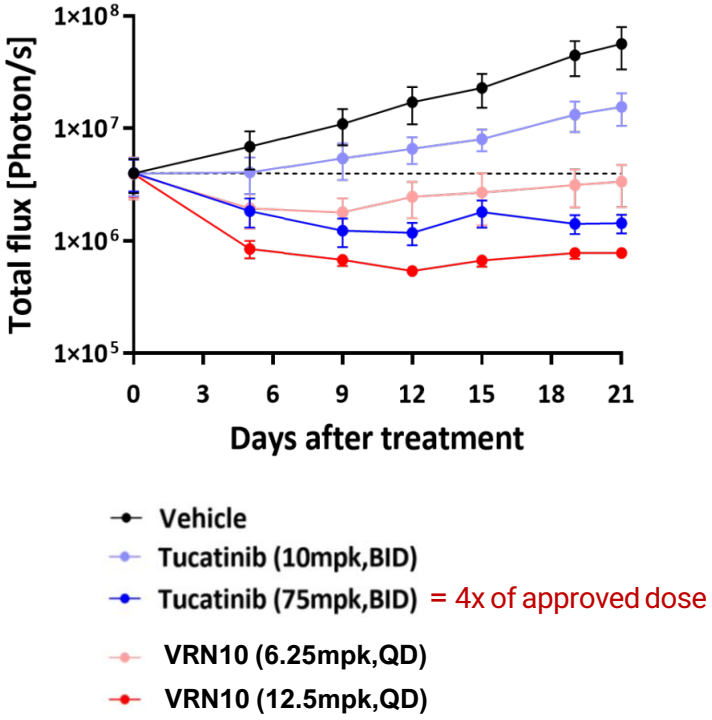


	VRN10	Tucatinib	Neratinib	Lapatinib
EGFR sparing (ratio to HaCaT GI50)	16~754	1~317	0~11	0~4

VRN10. Preclinical *in-vivo*: Brain metastasis

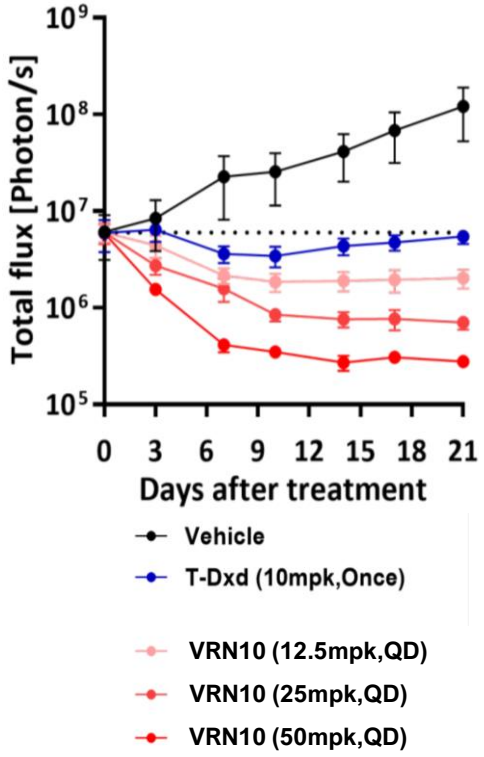
VRN10, Superior efficacy on HER2 positive intracranial(IC) xenograft model

BT474 (HER2+ breast;Tucatinib)

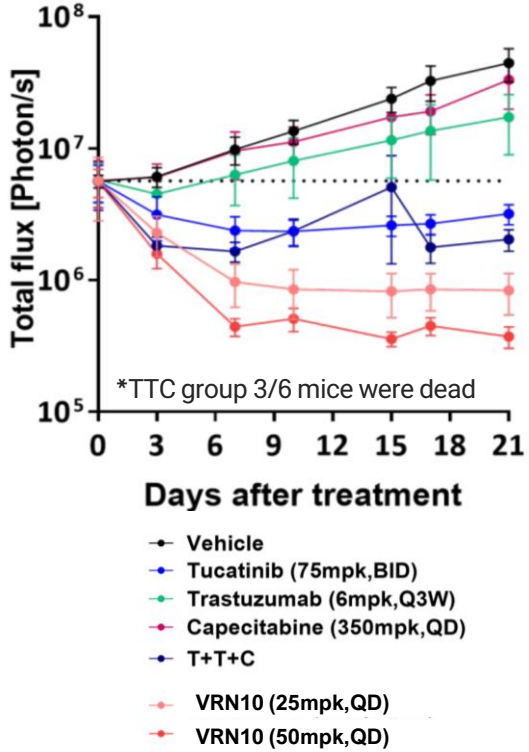


Current SOCs

BT474 (HER2+ breast; T-dxd)



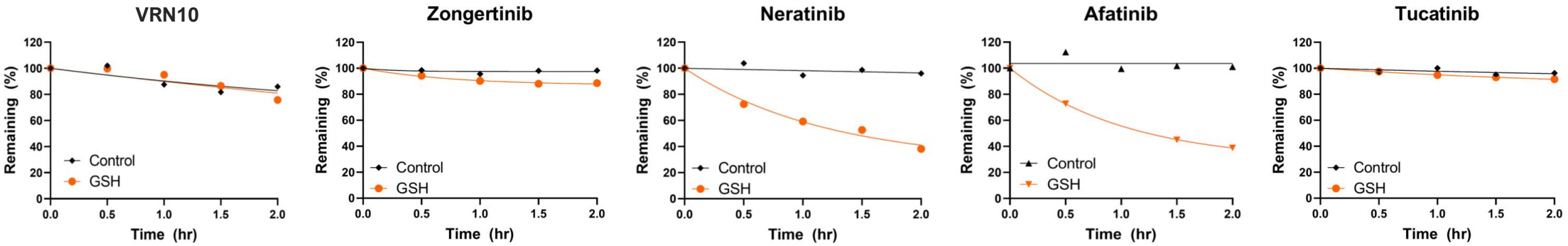
BT474 (HER2+ breast; T+T+C)



VRN10. Preclinical : GSH reactivity

Exposed to high chronic tox risk when intaking covalent inhibitor long term as it unwantedly binds to endogeneous detox substance GSH
Albeit covalent inhibitor, VRN10 has low risk of idiopathic chronic tox (i.e. liver tox, heme tox)

Less GSH reactivity anticipating less GSH depletion or cysteine modifications



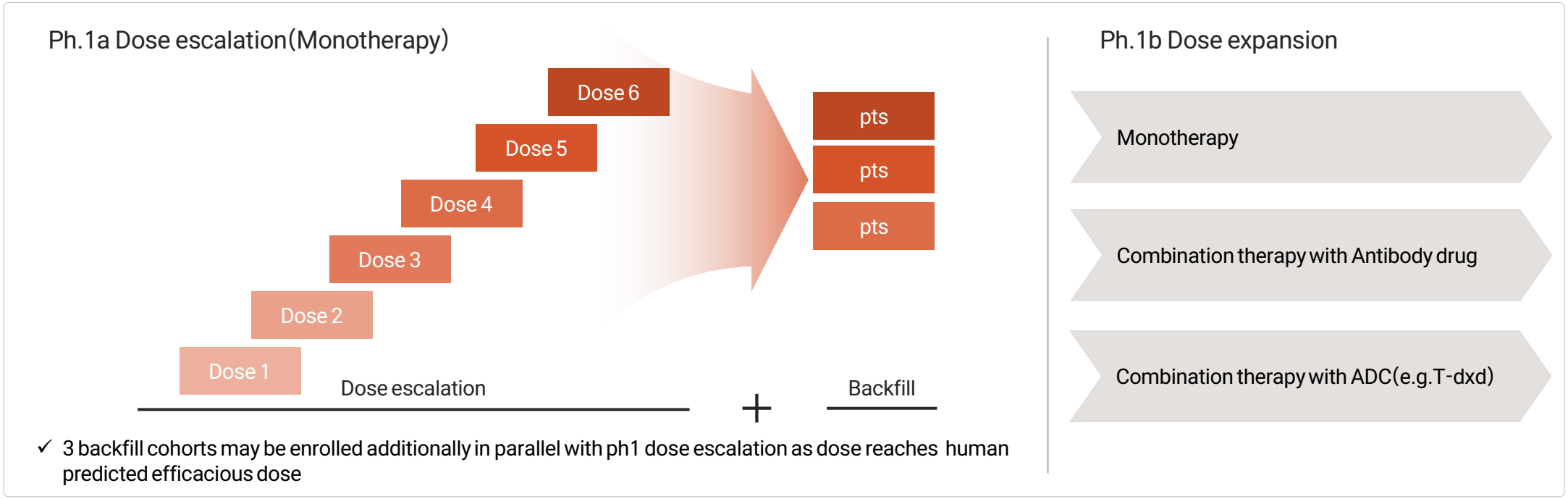
Type	Covalent HER2 specific				Covalent pan-ERBB				Non-covalent HER2 specific	
Half-life(hr)	VRN10		Zongertinib		Neratinib		Afatinib		Tucatinib	
	k	$T_{1/2}$ (hr)	k	$T_{1/2}$ (hr)	k	$T_{1/2}$ (hr)	k	$T_{1/2}$ (hr)	k	$T_{1/2}$ (hr)
Control	0.105	*6.6	0.007	*96.3	0.026	*26.5	0.058	*12.0	0.020	*35.0
GSH	0.140	*4.9	0.085	*8.1	0.449	1.5	0.474	1.5	0.044	*15.6
GSH – control	0.035	19.8	0.078	8.9	0.423	1.6	0.416	1.7	0.025	28.2

*Extrapolated value

VRN10. The first-in-human clinical study

Combination trial to be explored in ph1b

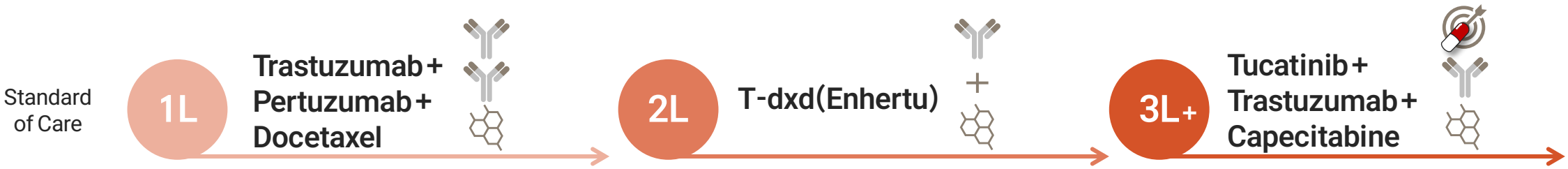
Phase 1 clinical trial design (up to N ~72)



✓ 3 backfill cohorts may be enrolled additionally in parallel with ph1 dose escalation as dose reaches human predicted efficacious dose

ENA2024 preclinical data presented,
Australia/Korea global ph1 in progress (AU IND approved), 1H 2025 first patient dosing expected

VRN10. HER2-positive Breast Cancer Market Landscape



Drug name (Brand name)	Trastuzumab (Hercepin)	Pertuzumab (Perjeta)	T-dxd (Enhertu)	Tucatinib (Tukysa)	ZN-A-1041
Company name	Roche	Roche	Astrazeneca Daiichi Sankyo	Seagen	Roche
Mechanism	Monoclonal Antibody	Monoclonal Antibody	ADC(Herceptin)	TKI	TKI
Peak sales	USD 7.1bn('18)	USD 4.3bn('21)	USD 13.8bn('30(E))	USD 1.4bn('30(E))	Zion-Roche Phase1, Out-licensing Total Deal value USD 610m

Source: Globaldata

Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design

VORONOI

Thank You