Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design

VORONOI

2024.06

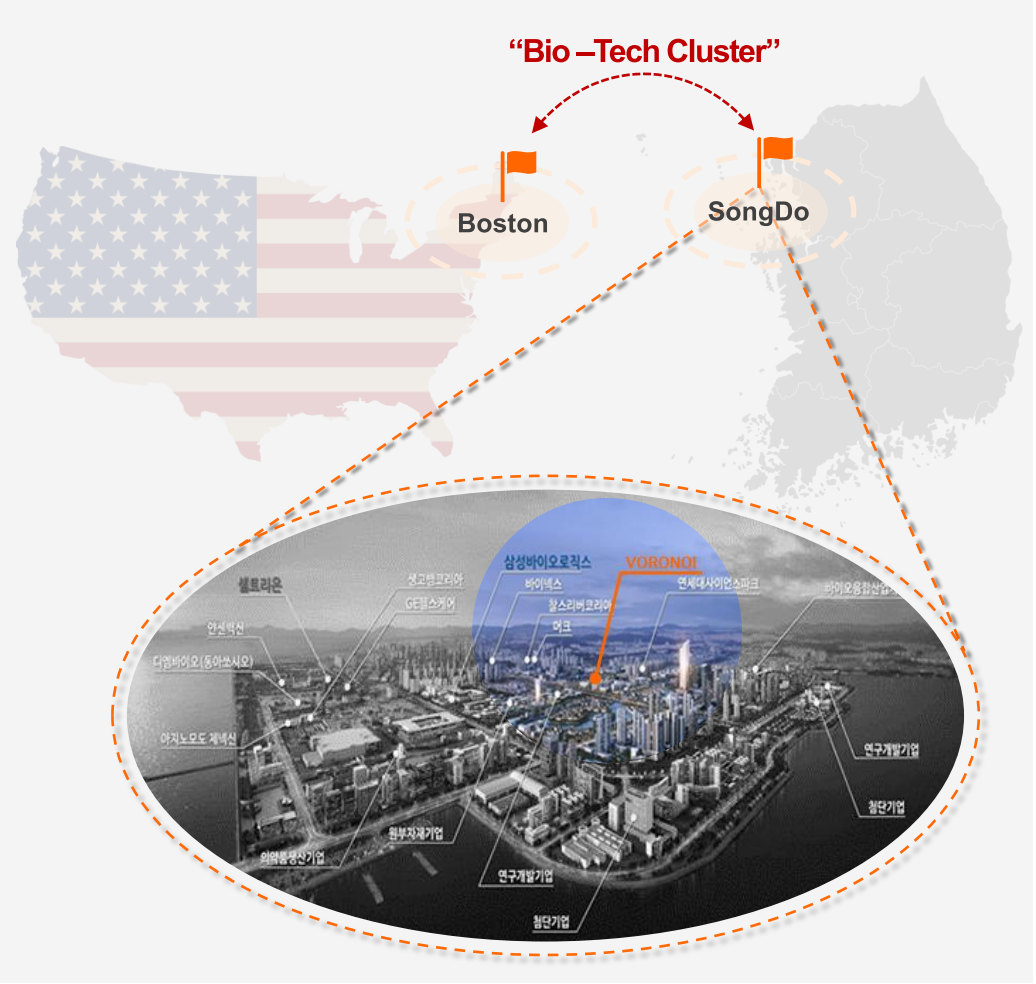
IR자료

VORONOI Overview

회사 요약

설립일	2015.02. (2022.06. KOSDAQ 상장)
대표자	김대권, 김현태
소재지	인천광역시 송도과학로 32
사업부문	신약개발
주요 연구분야	항암제 및 난치 질환 표적치료제
임직원 수 (2024.1Q)	127명
자본금 (2024.1Q)	89억원
자산 (2024.1Q)	937억원

회사 구조



주요 파이프라인

NDA 신청/제출 일정(예상)

회사명	적응증	타겟	임상단계			
			전임상	1상	2상	3상
ORIC	비소세포폐암	EGFR exon20 ins (treatment-naïve)				
		EGFR exon20 ins (post-amivantamab)				
		EGFR atypical				
		HER2 exon20 ins				
VORONOI	비소세포폐암	EGFR del19/C797S, EGFR L858R/C797S				
		EGFR del19, EGFR L858R (뇌 전이)				
		EGFR uncommon(2차)				
		EGFR del19, L858R, uncommon				
VORONOI	유방암	HER2+ positive				
inno.N	비소세포폐암	RET fusion				
VORONOI	자가면역질환	RIPK1				
VORONOI	폐동맥고혈압	PDGFR				

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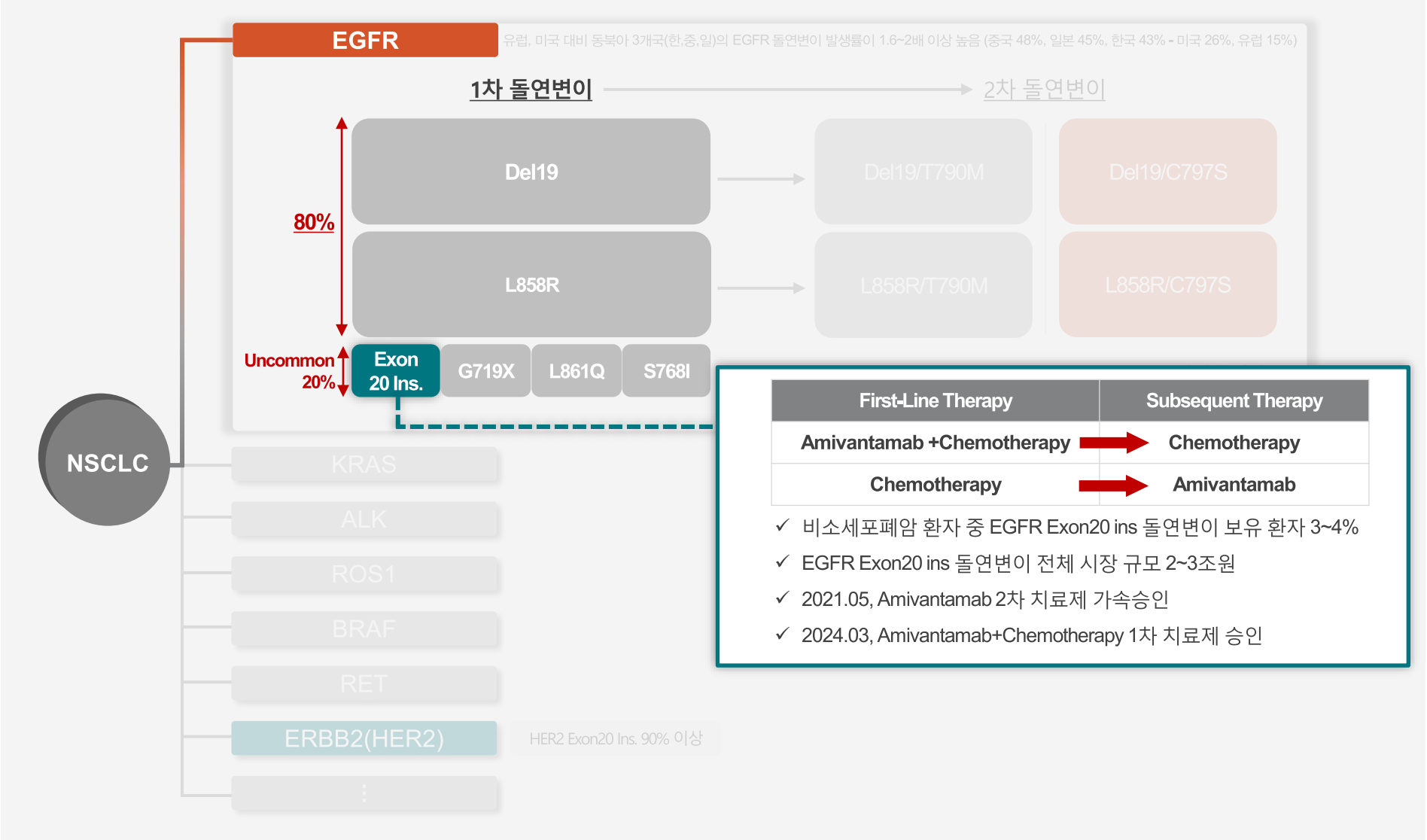
VORONOI

VRN07. EGFR Exon20 Insertion

Major Oncogenic Mutations for NSCLC(EGFR exon20 insertion)



First-Line Therapy		Subsequent Therapy
Amivantamab +Chemotherapy	→	Chemotherapy
Chemotherapy	→	Amivantamab

- ✓ 비소세포폐암 환자 중 EGFR Exon20 ins 돌연변이 보유 환자 3~4%
- ✓ EGFR Exon20 ins 돌연변이 전체 시장 규모 2~3조원
- ✓ 2021.05, Amivantamab 2차 치료제 가속승인
- ✓ 2024.03, Amivantamab+Chemotherapy 1차 치료제 승인

Efficacy

VRN07(ORIC-114). 2차 치료제로서의 효능 확인

Efficacy in 2nd Line EGFR Exon20 Insertion NSCLC

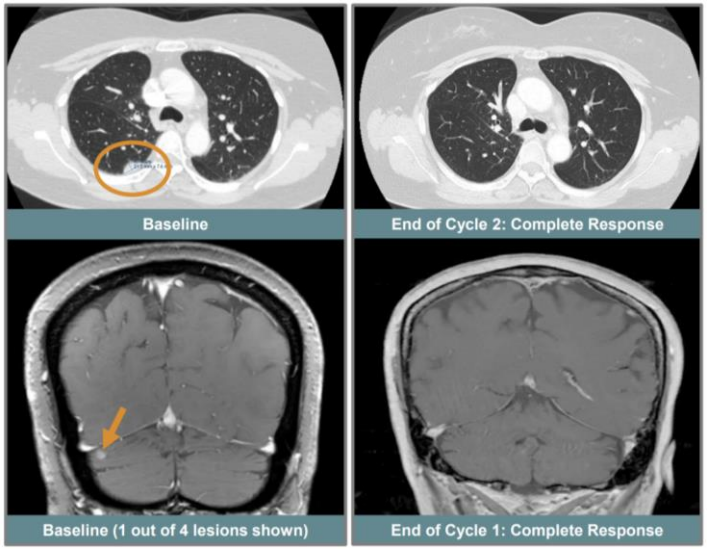
		Phase	N	with prior exon20 EGFR(%)	뇌전이 환자 (%)	CR	PR	ORR	PFS	비고
VORONOI ORIC	VRN07 ORIC-114	1a	21명	81%	86% (active 포함)	1+α명	3+α명	27+%	n/a	Untreated/ Active 뇌전이 환자 포함
janssen	Amivantamab	1	81명	1%	22%	3명	29명	40%	8.3개월	
Takeda	Mobocertinib	1/2	114명	0%	35%	0명	32명	28%	7.3개월	철회
ARRIVENT	Furmonertinib	1b	26명	n/a (7% EGFR)	29%	0명	12명	46%	7개월	
Dizal Pharma 迪哲医药	Sunvozertinib	2	97명	3% (amivantamab)	32%	0명	59명	46% (investigator)	~10개월 (추정)	
blueprint MEDICINES	BLU-451	1	48명	75%	58% (CNS disease)	-	-	-	-	개발 중단
cullinan ONCOLOGY	Zipalertinib	2	79명 100mg BID 39명	4%	38% (only stable)	0명	16명	41%	12개월	

출처: Cantor Fitzgerald Research (2024.02)

1. Heavily treated 환자 대상 유일한 완전 관해 임상 데이터

VRN07(ORIC-114). ESMO 2023

✓ **EGFR Exon20**

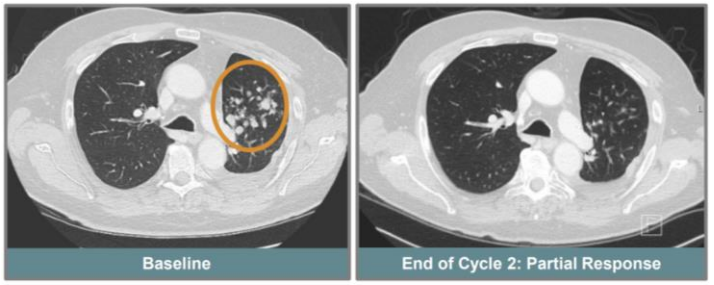


- **Patient: 55F with EGFR exon 20 mutated NSCLC**
- **Prior therapy:** Pemetrexed/cisplatin and amivantamab
- **CNS metastases at baseline:** Four active CNS non-target lesions
  - Previously untreated
  - No prior surgery
  - No prior radiation
- **ORIC-114 dose:** 75 mg QD
- **Systemic response:** Partial response after Cycle 1 (60% reduction of all target and non-target lesions) followed by complete response at the end of Cycle 2 (**100% reduction of all target and non-target lesions**), subsequently confirmed
- **CNS response:** Complete response after Cycle 1 (**100% reduction of all 4 CNS lesions**), confirmed after Cycle 2
- **Grade ≥2 treatment-related AEs:** Grade 2 mucositis and paronychia
- **Duration of treatment:** Cycle 9 (ongoing)

✓ Chemotherapy, Amivantamab 치료 이후의 환자

✓ Cycle 2, 전신 완전 관해
Cycle 1, CNS 완전 관해

✓ **HER2 Exon20**



- **Patient: 67M with HER2 exon 20 mutated NSCLC**
- **Prior therapy:** Pemetrexed/cisplatin, ipilimumab/nivolumab/carboplatin, and pemetrexed/carboplatin/pembrolizumab
- **ORIC-114 dose:** 30 mg BID
- **Systemic response:** Partial response after Cycle 1 (**100% reduction of all target lesions**; non-target lesions non-CR/non-PD), confirmed at the end of Cycle 2 (**100% reduction of all target lesions**)
- **Grade ≥2 treatment-related AEs:** Grade 2 rash and nausea
- **Duration of treatment:** Cycle 3 (ongoing)

✓ 3번의 항암치료 실패 환자

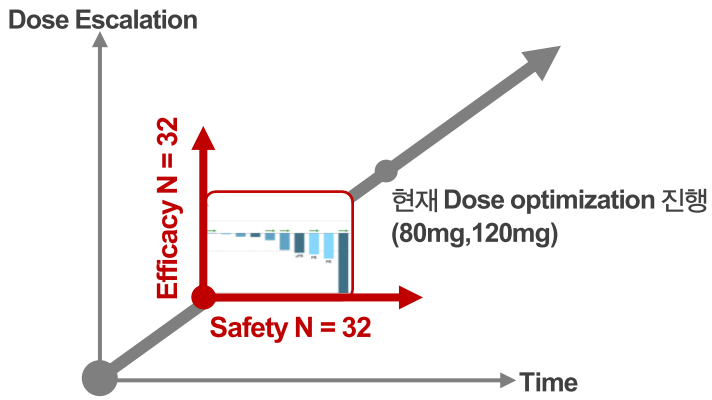
✓ 전신 완전 관해 도달

출처: ESMO2023

2. Amivantamab 이후의 치료 효과를 보여준 유일한 임상 데이터

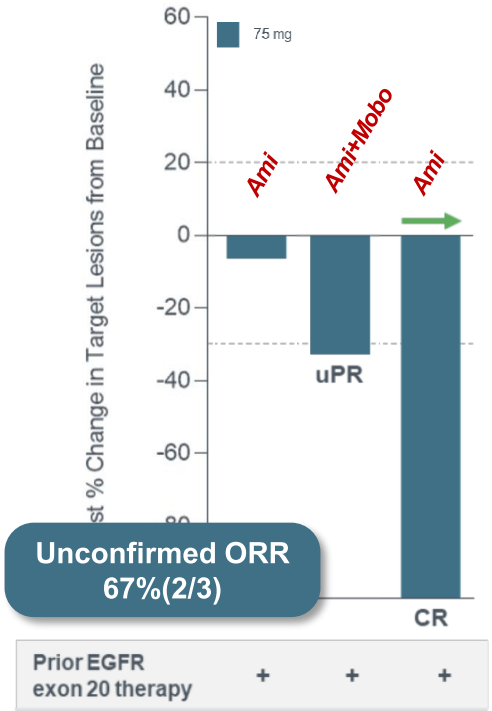
VRN07(ORIC-114). ESMO 2023

VRN07(ORIC-114) 진행 상황



대상 환자군	Heavily treated 환자 대상 ✓ With prior Exon20 EGFR 81% ✓ Chemo → Ami → (Mobo or Blu-451 등) ✓ 초기 환자 모집에서부터 뇌전이 환자 86%

EGFR Exon20 ins NSCLC 2차 치료제 임상 데이터 비교



With Prior Exon20 EGFR 81%

	ARRIVENT	Dizal Pharma	cullinan ONCOLOGY
	Furmonertinib	Sunvozertinib	Zipalertinib
with prior exon20 EGFR(%)	n/a (7% EGFR)	3% (amivantamab)	4%
CR	0명	0명	0명
ORR	46%	46% (investigator)	41%
PFS	7개월	~10개월 (추정)	12개월

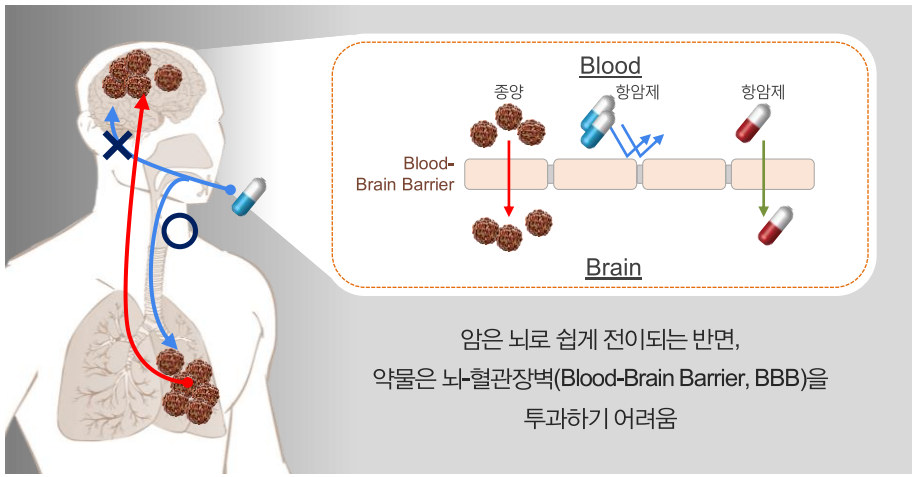
✓ Amivantamab 이후의 치료 효과 확인
✓ 경쟁 약물 대비 2차 치료제로서의 우수한 효능

출처: ESMO2023

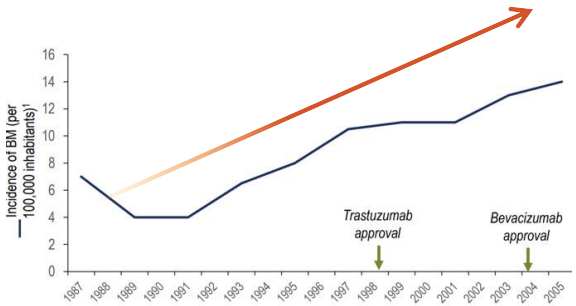
EGFR 표적치료제 뇌혈관장벽 투과율

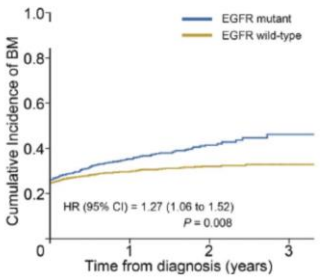
뇌전이 환자에 대한 미충족 의료 수요 존재

약물의 뇌혈관장벽 투과율 낮은 이유



암의 뇌전이 발생률





NSCLC 뇌전이 발생률

Indian Journal of CANCER

Management of CNS metastases in patients with EGFR mutation-positive NSCLC

Shetty, Vijith; Babu, Suresh[1]

Central nervous system (CNS) metastases are a major complication associated with non-small cell lung cancer (NSCLC) and are seen in >30% of patients.[1,2] About 25% of patients with NSCLC have CNS metastases at initial presentation, whereas 80% of patients develop it within 2 years of NSCLC diagnosis.[3] The rising incidence of CNS metastases in NSCLC is probably due to better control of extracranial disease and increase in detection rates of asymptomatic CNS metastases with improved magnetic resonance imaging techniques.[4] This review compares the efficacy and safety of various available options in the management of NSCLC with CNS metastases.

➔40% 이상의 뇌전이 환자 중 처음 진단 받으면서 이미 뇌전이있는 환자 25% 이상, 진단 2년 이내에 80% 환자 뇌전이 발생

출처: FDA website, Globaldata, Neuro-Oncology, Brain metastasis ESMO 2019
Shetty, Vijith; Babu, Suresh1. Management of CNS metastases in patients with EGFR mutation-positive NSCLC. Indian Journal of Cancer 56(Suppl 1):p S31-S37, November 2019. | DOI: 10.4103/ijc.IJC_455_19

EGFR 표적치료제 뇌혈관장벽 투과율

승인된 치료제 대비 높은 뇌혈관장벽 투과율을 가진 VRN07(ORIC-114)

기존 EGFR TKIs의 뇌혈관장벽 투과율

Preclinical Comparison of the Blood–brain barrier Permeability of Osimertinib with Other EGFR TKIs

Nicola Colclough, Kan Chen, Peter Johnström, Nicole Strittmatter, Yumei Yan, Gail L. Wrigley, Magnus Schou, Richard Goodwin, Katarina Varnäs, Sally J. Adua, Minghui Zhao, Don X. Nguyen, Gareth Maglennon, Peter Barton, James Atkinson, Lin Zhang, Annika Janefeldt, Joanne Wilson, Aaron Smith, Akihiro Takano, Ryosuke Arakawa, Mikhail Kondrashov, Jonas Malmquist, Evgeny Revunov, Ana Vazquez-Romero, Mohammad Mahdi Moein, Albert D. Windhorst, Natasha A. Karp, M. Raymond V. Finlay, Richard A. Ward, James W.T. Yates, Paul D. Smith, Lars Farde, Zack Cheng, and Darren A.E. Cross

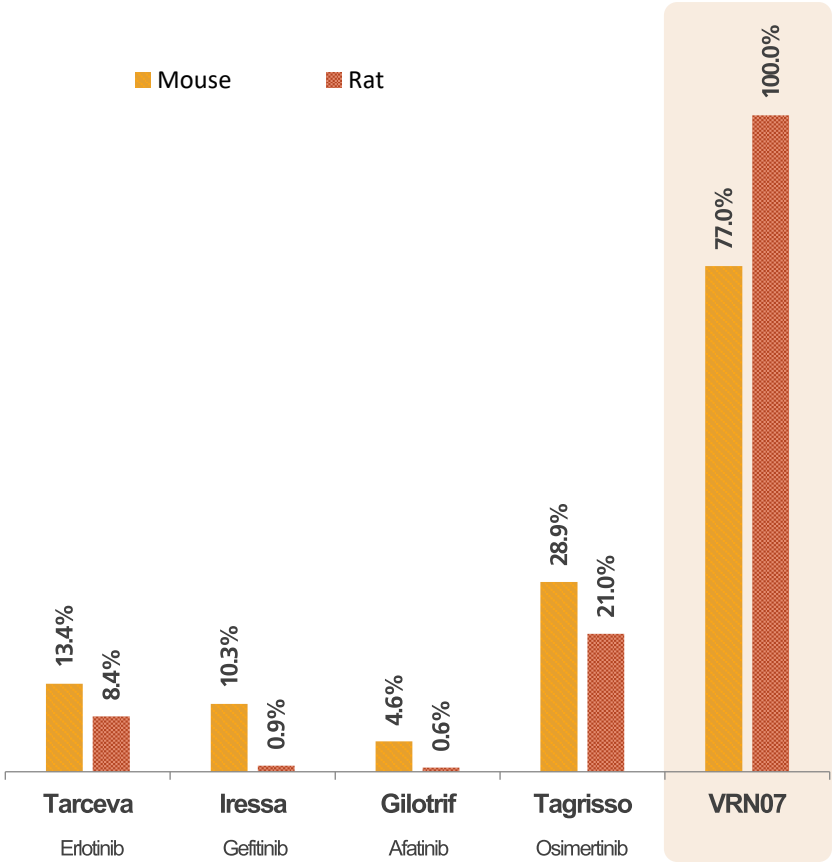
DOI: 10.1158/1078-0432.CCR-19-1871 Published January 2021

Table 2.
Summary of healthy rat brain and CSF distribution constants, Kp and Kpuu, plus brain and plasma binding, fuplasma and fubrain, for 16 EGFR-TKIs.

Drug	Brain Kp	CSF Kp	fuplasma %	fubrain %	Brain Kpuu	CSF Kpuu	
Osimertinib	6.09	0.0047	1.66 (0.22)	0.057 (0.012)	21.0%	29.0%	Tagrisso
Icotinib	0.17	0.051	8.38 (0.15)	6.06 (0.77)	12.0%	61.0%	
Lazertinib	1.17	ND	1.70 (0.35)	0.126 (0.018)	8.7%	ND	Leclaza
Avitiniba	0.12	NV	0.87 (0.06)	0.623 (0.066)	8.6%	NV	
Erlotinib	0.14	0.034	8.77 (0.19)	5.18 (0.55)	8.4%	39.0%	Tarceva
Poziotinib	0.07	0.00068	1.10 (0.30)	0.912 (0.092)	6.0%	6.2%	
Naquotinib	0.24	0.014	6.98 (1.61)	0.974 (0.192)	3.4%	20.0%	
Dacomitinibb	0.76	0.0085	4.04 (0.27)	0.157 (0.023)	3.0%	21.0%	
Tesevatinib	0.99	0.0042	3.39 (0.50)	0.087 (0.008)	2.5%	12.0%	
AZ'5104	0.32	0.0056	5.64 (0.22)	0.335 (0.064)	1.9%	9.9%	
Olmutinib	0.12	NV	1.18 (0.59)	0.117 (0.016)	1.2%	NV	
Gefitinib	0.12	0.0074	4.38 (0.82)	0.341 (0.070)	0.9%	17.0%	Iressa
Rociletinib	0.008	NV	2.10 (0.61)	1.98 (0.07)	0.8%	NV	
Afatinib	0.2	0.024	9.48 (0.75)	0.297 (0.031)	0.6%	26.0%	Gilotrif
Nazartinibc	0.041	0.0071	8.94 (0.72)	1.00 (0.10)	0.5%	7.9%	

Note:
Kp determined from AUC brain/plasma and AUC CSF/plasma ratios using 6 rats per compound with one terminal sample per time point (Eq. 2) with Kpuu determined by factoring in tissue binding to Kp using Eqs. (3) and (4).
NV—no value determined—compound detected at only one or two time points.
Fraction unbound in plasma fuplasma and fraction unbound in brain fubrain average of n = 3; (SD)

EGFR 치료제의 뇌-혈관장벽 투과율 (Kp,uu, Brain/ Mouse, Rat)



출처: Nicola Colclough et al. Clin Cancer Res 1 January 2021; 27 (1): 189–201.

3. Active 뇌전이 환자에 대한 치료 효과를 확인한 최초 임상 데이터

Active brain metastases – EGFR 치료제 중 임상 최초

기존 EGFR 폐암 표적치료제 임상 한계

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).

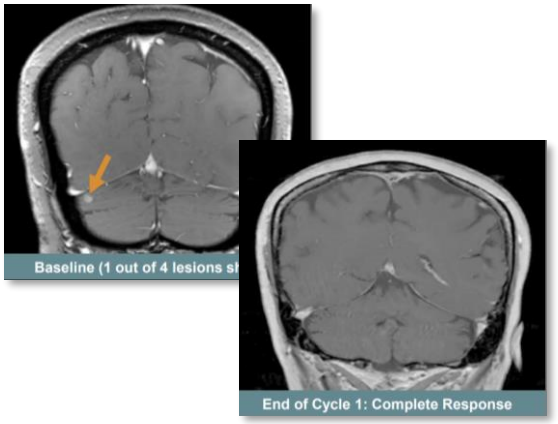
VRN07(ORIC-114), Patient Population

- 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 뇌전이 환자 포함한 임상 환자 모집

VRN07(ORIC-114), Active 뇌전이환자 완전관해 최초 사례

	뇌전이 환자 (%)
VRN07 ORIC-114	86 (active 포함)
Amivantamab	22
Mobocertinib	35
Furmonertinib	29
Sunvozertinib	32
BLU-451	58 (개발 중단)
Zipalertinib	38 (only stable)



- **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

뇌전이 환자 13명 중 총 8명 효능 확인

✓ **CR 1명**

✓ **PR / SD 7명**

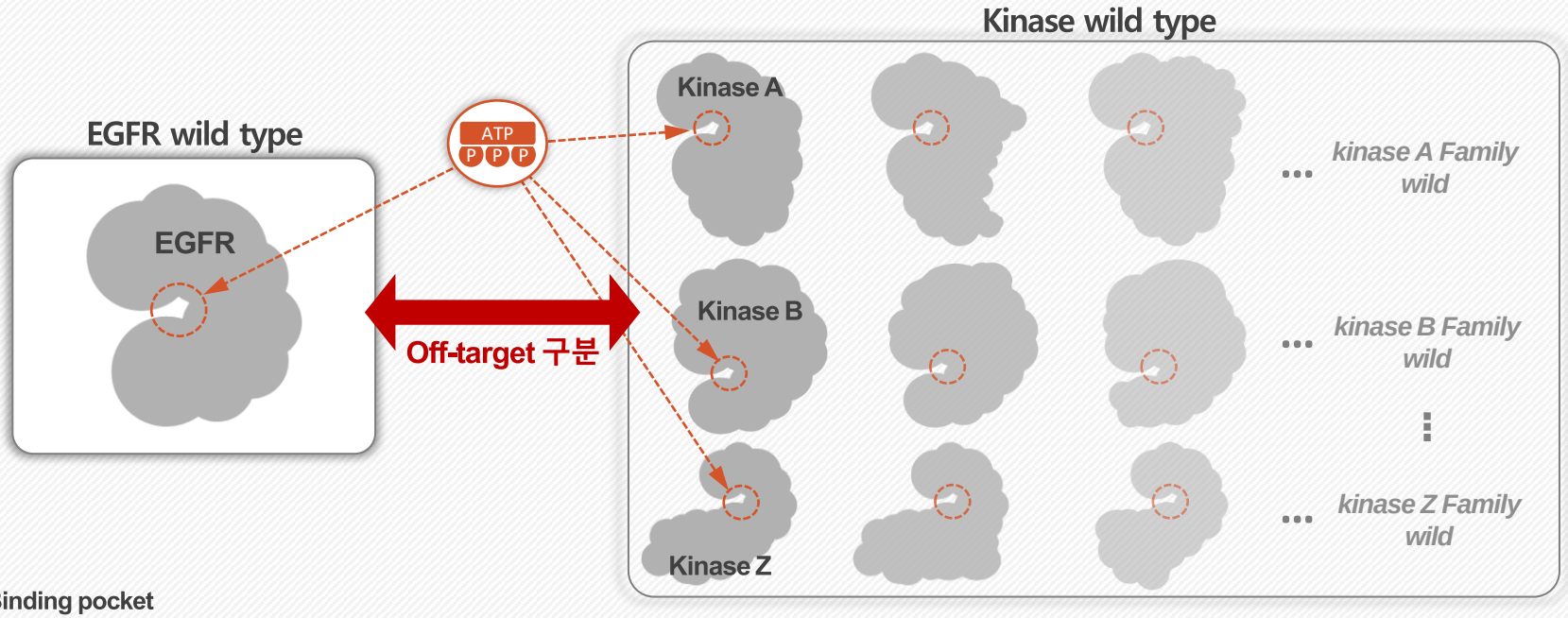
Active 뇌전이 환자에서 CR 사례 최초 확인

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

Toxicity

Off-target Toxicity

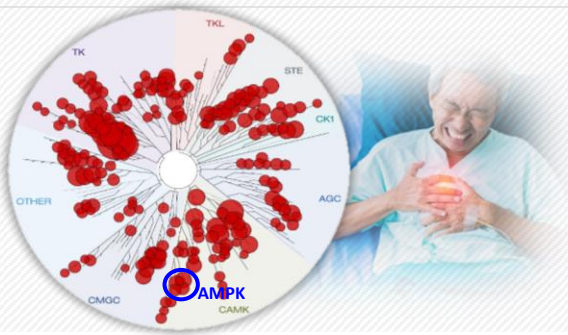
Off-target Example



Off-target Toxicity

- 혈관 및 종양세포의 여러 효소를 표적으로 하는 Sunitinib의 AMPK 억제로 인한 심독성 논문

> Sunitinib-induced cardiotoxicity is mediated by off-target inhibition of AMP-activated protein kinase



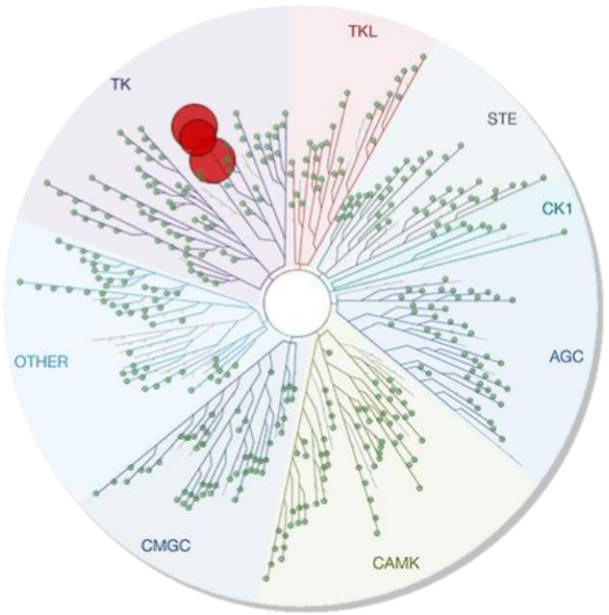
출처: Freepik(Lifestylememory)

VRN07(ORIC-114). Selectivity

비소세포폐암 EGFR Exon20 insertion 타겟 치료제 사례

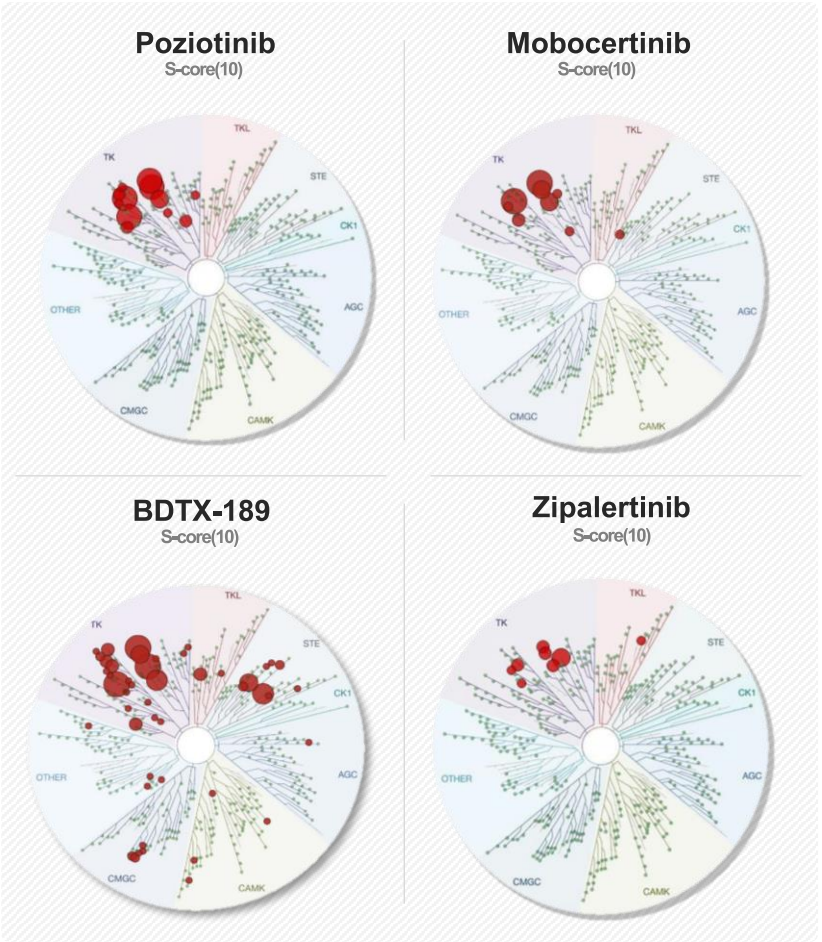
VRN07(ORIC-114)

(1 μM, top 10%)



Off-target toxicity (%): 0

- 빨간색 원은 Kinase 결합력을 나타냄



출처: AACR2022

4. Off-target 독성이 없는 최초의 임상 데이터

VRN07(ORIC-114). Off-target Toxicity

Clinical trial. Off-target Toxicity data[1,2,3,4,5,6]

약물명		Grade ≥3 부작용	
	N	Total	Off-target Toxicity
Amivantamab[1] (Monotherapy)	114	35%	IRR 3%, decreased lymphocytes 8%, dyspnea 2%, Interstitial lung disease, ocular toxicity
Amivantamab + Chemotherapy	130	72%	IRR 5%, Neutropenia 45%, Thrombocytopenia 15%, Anemia 12%, Leukopenia 20%
Sunvozertinib	104	39%	Blood Creatine phosphokinase increased 17.3%, Lipase increased 1.9%, anemia 5.8%, Lipase increased 1.9%
Furmonertinib	28	29%	Anemia 4%, Electrocardiogram QT prolonged 7%, liver toxicity(ALT increased) 4%
Zipalertinib	73	53%	Anemia 9.6%, liver toxicity(AST increased) 4%
ORIC-114 (VRN07)	32	19%*	X

출처: [1]Keunchil Park et al., JCO 39, 3391-3402(2021), FDA RYBTRVANT Label [2]ESMO2023, [3]A. Passaro et al., Annals of Oncology, Volume 35, Issue 1,2024., [4]ASCO2023, [5]WCLC2023, [6]Zofia Piotrowska et al., JCO 41, 4218-4225(2023). *유효 용량 이상의 부작용 데이터

VRN07(ORIC-114), EGFR Exon20 Ins. 비소세포폐암 2차 치료제 기대

EGFR Exon20 Ins. 비소세포폐암 2차 치료제로서의 가능성 확인

1. Heavily treated 환자 대상 유일한 **완전 관해(CR)** 임상 데이터
2. **Amivantamab 불응 환자의 치료 효과**를 보여준 유일한 임상 데이터
3. **Active 뇌전이 환자에 대한 치료 효과**를 확인한 최초 임상 데이터
4. **Off-target 독성**이 없는 최초의 임상 데이터

VRN07(ORIC-114). 1차 치료제 시장으로 확장

Treatment-naïve 환자 대상 확장 코호트 개시

ORIC

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

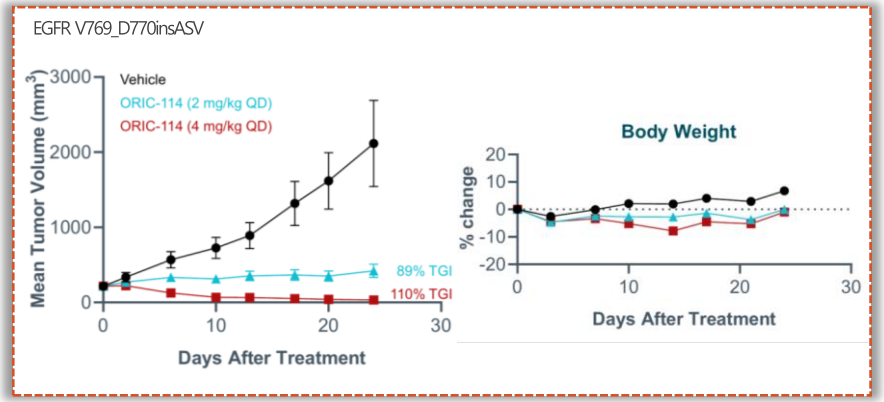
April 15, 2024 at 4:15 PM EDT

Initiated multiple Phase 1b expansion cohorts to determine the RP2D of ORIC-114 in NSCLC patients with EGFR exon 20, HER2 exon 20, or EGFR

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

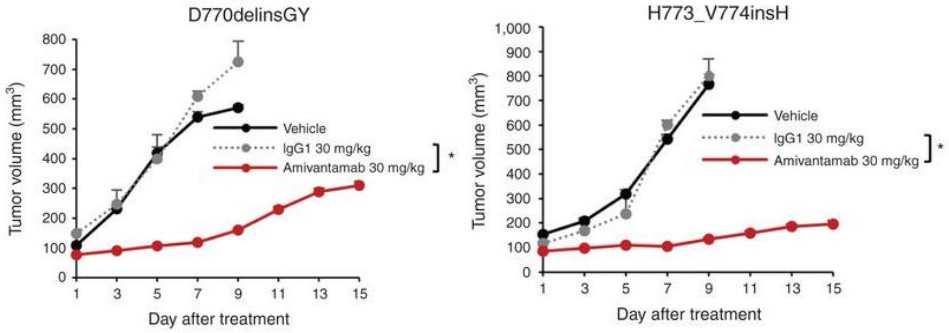
stage oncology company focused on developing treatments that address mechanisms of therapeutic resistance, today announced the completion of the dose escalation portion of the Phase 1b trial of ORIC-114 in patients with advanced solid tumors with EGFR and HER2 exon 20 alterations or HER2 amplifications. Based upon these data, ORIC selected the two provisional recommended Phase 2 dose (RP2D) levels of ORIC-114 at 80 mg and 120 mg QD, which are being further evaluated in three dose expansion cohorts for dose optimization and final RP2D selection. These expansion cohorts have now been initiated in patients with non-small cell lung cancer (NSCLC) with EGFR exon 20 (EGFR exon 20 inhibitor naïve), HER2 exon 20, or EGFR atypical mutations. The company also announced the initiation of an extension cohort for the treatment of patients with first-line, treatment-naïve EGFR exon 20 NSCLC.

VRN07(ORIC-114)



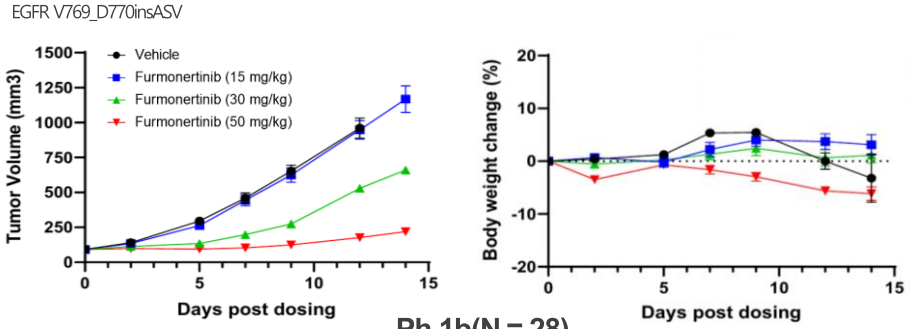
EGFR Exon20 insertion 타겟 치료제 데이터 비교

Amivantamab



Ph.3(Ami+chemo vs chemo, N = 308)
ORR 73%, PFS 11m
Grade ≥3 AEs 75%

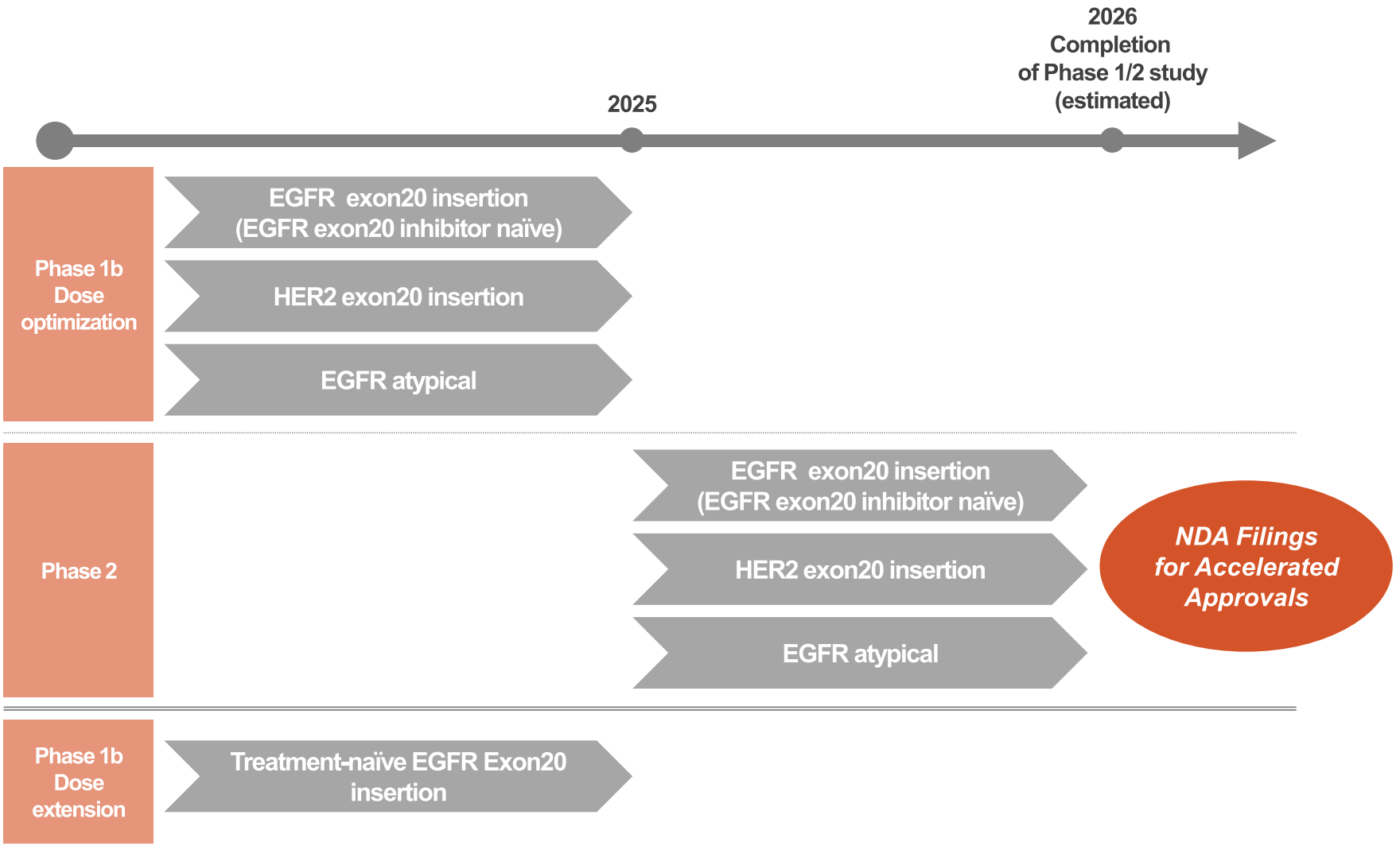
Furmonertinib



Ph.1b(N = 28)
ORR 79%, PFS 11m
Grade ≥3 AEs 13~29%

출처: ORIC, AACR2021, IASLC2022, WCLC2023, ESMO2023, Jiyeon Yun et al., Cancer Discov 1 August 2020; 10 (8): 1194–1209

VRN07(ORIC-114). Planned Next Steps



VRN07(ORIC-114). 전문가의 평가 바탕 파이프라인 가치 예상

2026
Completion
of Phase 1/2 study
(estimated)

NDA
Filings

약 2조5,000억원 예상

ORIC

Development milestone
1억 5,800만 달러

Sales milestone
4억 5,000만 달러

✓ Total milestone 약 7,900억원

Royalty

✓ 연간 Royalty[1] 400억~500억원 추정(x25년)
➔ 최소 1조원 이상 추정 가능

Milestone

✓ 중화권 매출 예상 규모 2,000억원
글로벌 Peak sales[1]의 20% 가정

✓ 중화권 판권 마일스톤 예상 규모 4,000억원
글로벌 Peak sales[1]의 2배수 가정

Royalty

✓ 연간 Royalty 140억 추정(x25년)
➔ 약 3,400억원 추정 가능

해외 증권사[1]의 파이프라인 평가를 통해 추정
Market share 30% 가정, EGFR exon20 ins. 1차 치료제 시장 미포함

출처: 1) Peak Sales(Cantor Fitzgerald Research (2024.02)), Net Sales to Gross Sales 85% 가정, Royalty 비율: high single 가정
$1 = ₩1,324(서울외국환중개 2024년 1월 매매기준율 평균

VRN07(ORIC-114). Reference Deal

1. Cullinan Oncology(CGEM) – Taiho Pharmaceutical Deal:

- ✓ 2022년, Cullinan Oncology이 Taiho Parmaceutical에 기술이전한 임상 1/2상 단계의 Zipalertinib(CLN-081/TAS6417)
- ✓ 계약금 2억 7,500만 달러 + 마일스톤 1억 3,000만 달러로, 총 4억 500만 달러의 계약 규모
  (미국 Sales의 50% 및 일본/중국 제외한 글로벌 권리 100%)

2. Blueprint Medicines(BPMC) – Lengo Therapeutics 인수:

- ✓ 전임상 단계(IND ready asset)의 BLU-451(LNG-451) 포함
- ✓ 계약금 2억 5,000만 달러 + 허가, 판매 마일스톤 2억 1,500만 달러로, 총 4억 6,500만 달러의 규모
- ✓ 2024년 개발 중단

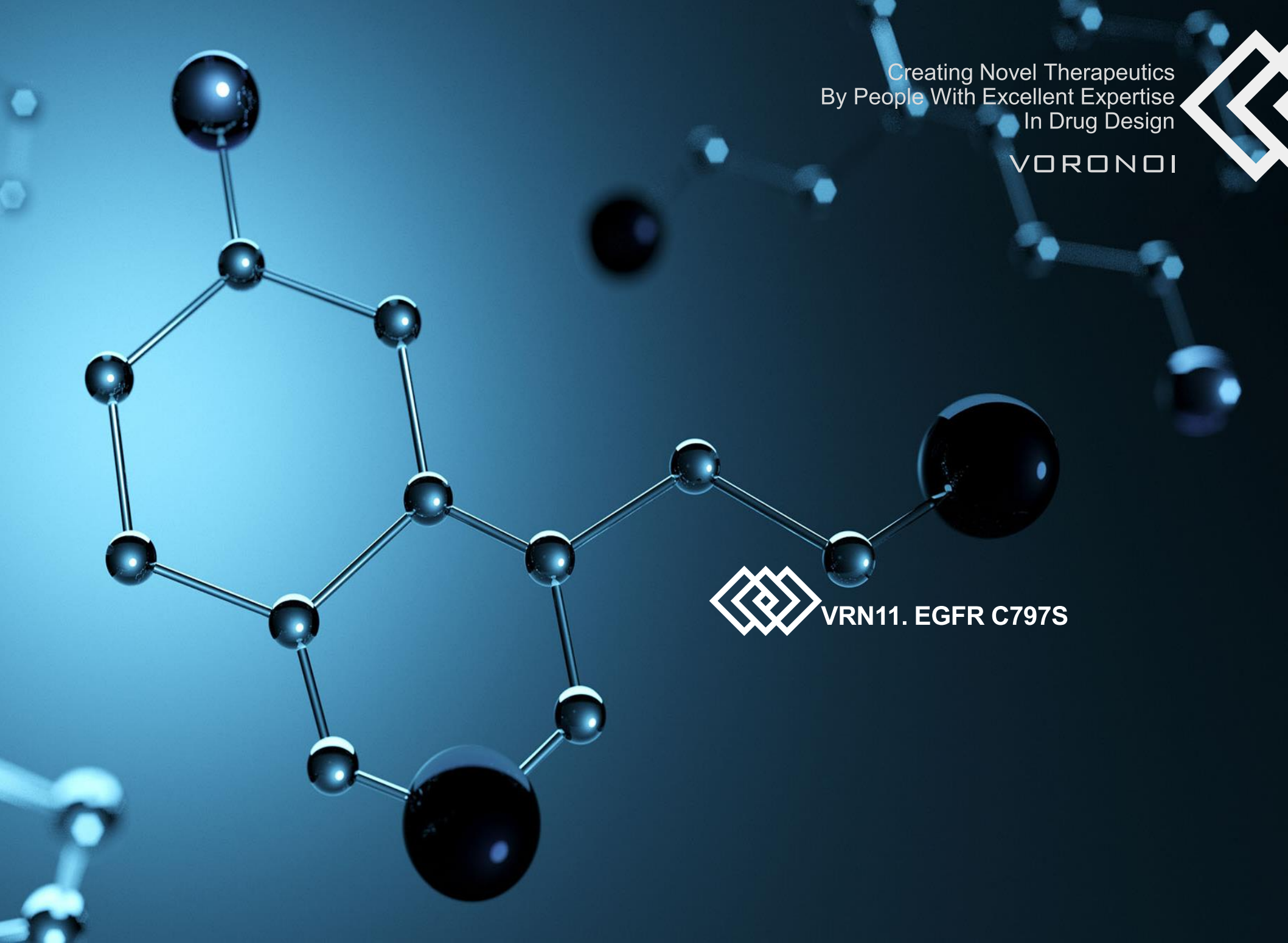
3. Arrivent Biopharma(AVBP) 2024년 NASDAQ 상장:

- ✓ 임상 3상 중인 Furmonertinib(EGFR/HER2 Exon20 ins 타겟 비소세포폐암 치료제)을 바탕으로 상장
- ✓ 상장 당시 시가총액 7억만 달러

출처: Cantor Fitzgerald Research (2024.02)

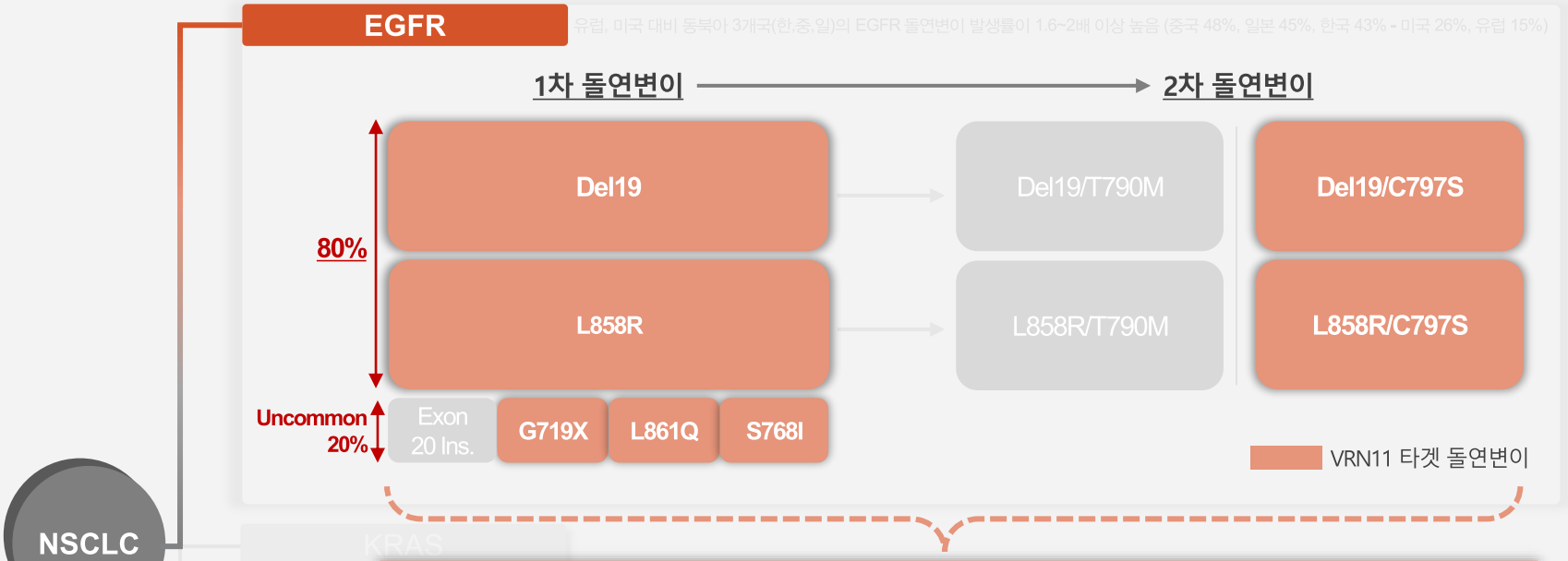
Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design

VORONOI



VRN11. EGFR C797S

Major Oncogenic Mutations for NSCLC

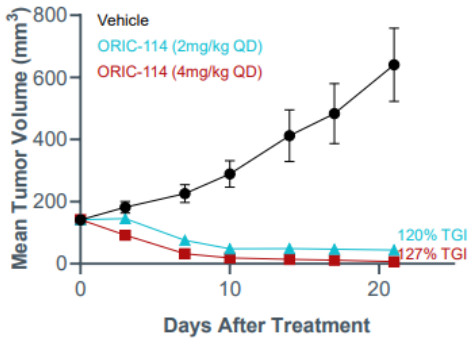


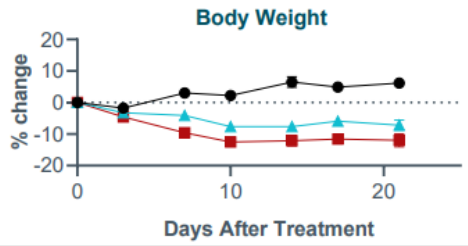
Mutations	First-Line Therapy	Subsequent Therapy
Del19, L858R	Tagrisso	뇌 전이 환자, 미충족 의료 수요 존재
G719X, L861Q, S768I	Gilotrif, Tagrisso	뇌 전이 환자, 미충족 의료 수요 존재
Del19/C797S, L858R/C797S	승인 치료제 부재	

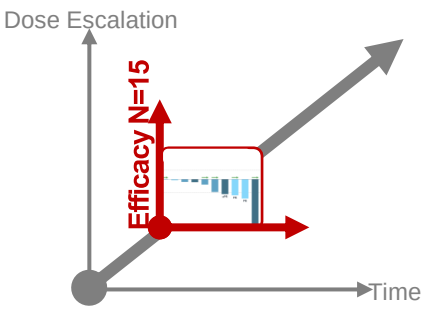
- ✓ EGFR Del19, L858R 돌연변이 시장 규모 10조원 이상
- ✓ EGFR uncommon 돌연변이(G719X, L861Q, S768I) 시장 규모 2~3조원
- ✓ EGFR C797S 돌연변이 시장 규모 2조원 이상
- ✓ 비소세포폐암 환자 중 뇌 전이 발생 비율 30~40% 이상

VRN07 & VRN11. *in-vivo & Clinical trial*

VRN07(ORIC-114)



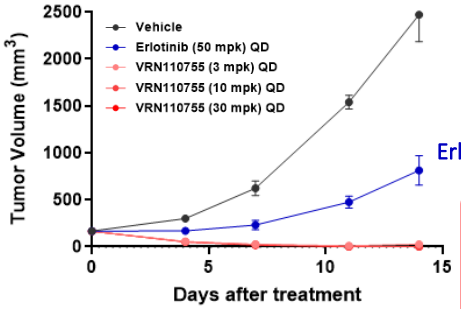




PR 3/15
CR 1/15
SD 4/15

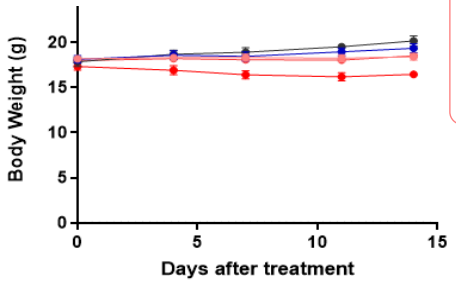
DOR 53.3%

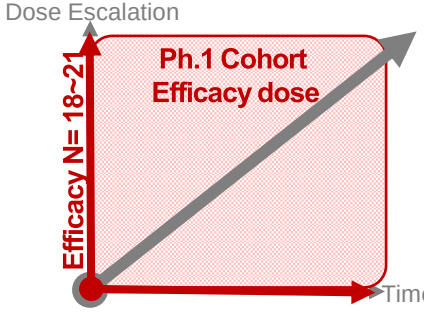
VRN11



Erlotinib 50mpk

CR	CR	CR
3 mpk	10 mpk	30mpk
x1	x3	x10
3 mpk	10 mpk	30mpk



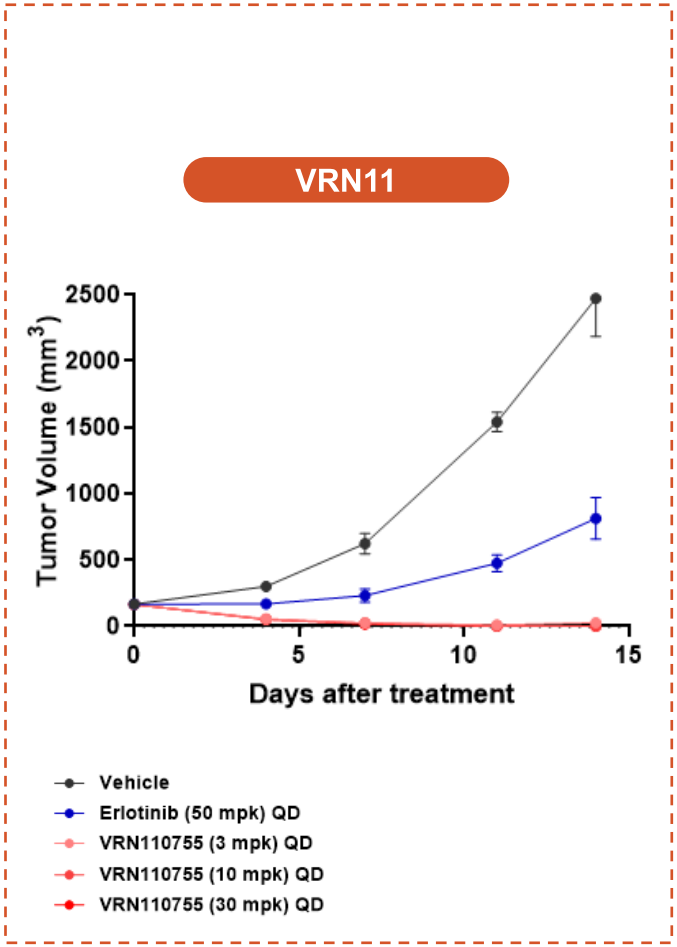


2024년 3월
환자 투약 시작

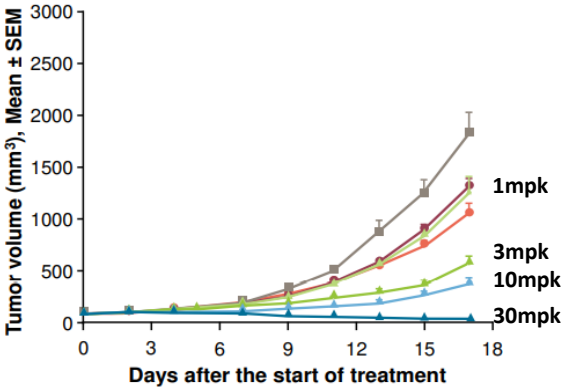
출처: AACR2021

VRN11. Competitive landscape

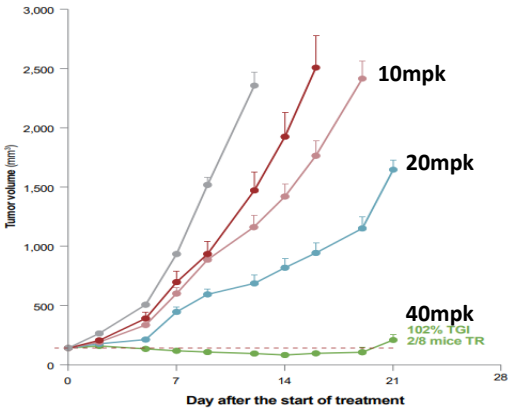
현재 EGFR C797S에 대한 치료제가 부재한 가운데, 경쟁 약물 대비 뛰어난 효능 확인



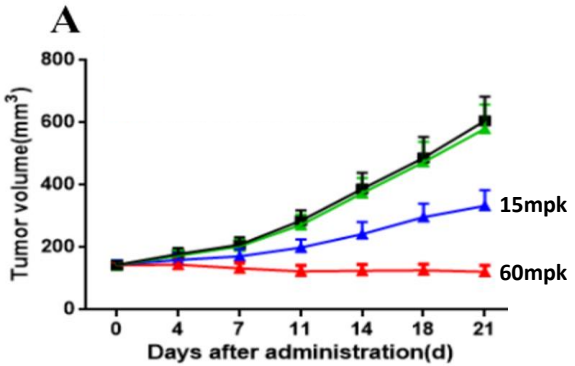
B사 B약물



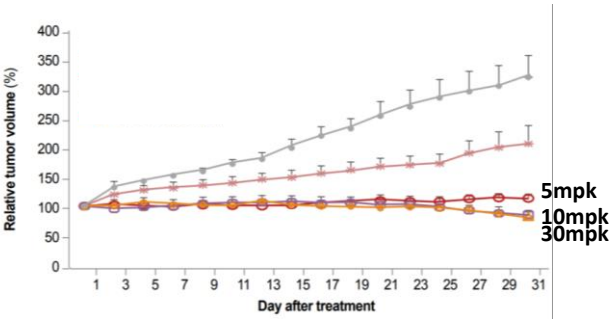
B`사 B`약물



Q사 Q약물



B`사 B``약물

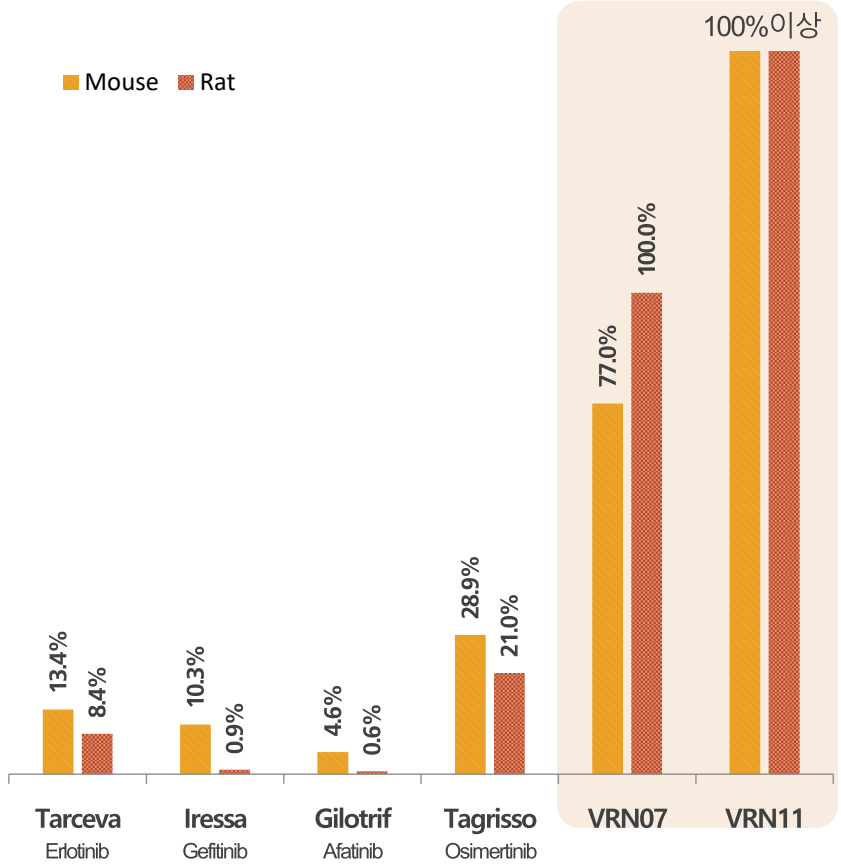


출처: AACR2021, AACR2022, ESMO2021, AACR-NCI-EORTC2023

VRN11. EGFR 표적치료제 뇌혈관장벽 투과율

승인된 치료제 대비 높은 뇌혈관장벽 투과율 확인
이를 바탕으로 한 뇌전이 환자 포함한 임상 설계

EGFR 치료제의 뇌-혈관장벽 투과율 (Kp,uu, Brain/ Mouse, Rat)



뇌전이, 연수막 전이 환자를 포함하는 공격적인 임상 설계

Del19, L858R, C797S, uncommon 돌연변이
또는 복합 돌연변이를 포함한
EGFR 활성화 돌연변이가 있는 NSCLC

+

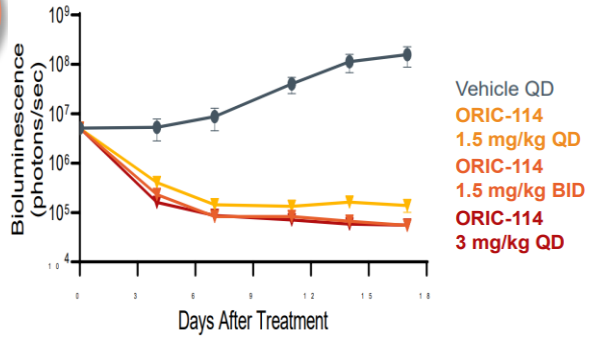
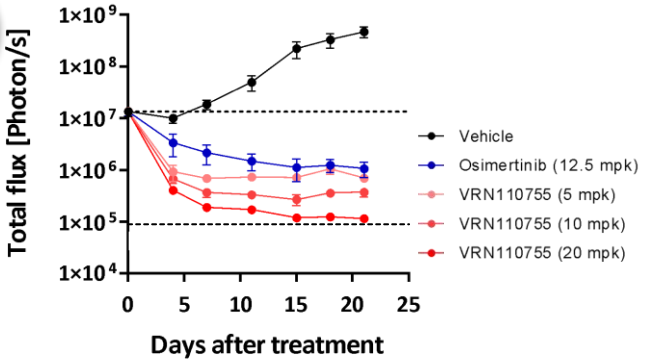
Include
Brain metastasis(BM)
and Leptomeningeal metastasis(LM) patients
- untreated and asymptomatic patients
- treated and controlled* patients

controlled : 뇌전이로 인한 증상을 steroid 10mg/daily로 조절 가능한 환자

출처: Nicola Colclough et al. Clin Cancer Res 1 January 2021; 27 (1): 189–201.

VRN07 vs VRN11. Active CNS Metastases

VRN07을 통해 Active brain metastases 환자군에서의 효능 확인 및 VRN11에서의 치료 효과 기대

	VRN07(ORIC-114)	VRN11
In-vivo Data	77% 투과 	100% 투과 
타겟	EGFR Exon20 Ins.	EGFR del19, EGFR L858R EGFR del19/C797S, EGFR L858R/C797S EGFR uncommon mutation
BM Patients	Inclusion of patients with active brain metastases	Inclusion of patients with active brain metastases
Clinical trial Data	뇌전이 환자 n =13 CR 1 PR / SD 7	*2023년 10월 한국 임상1상 IND 승인* *2024년 01월 대만 임상1상 IND 승인*

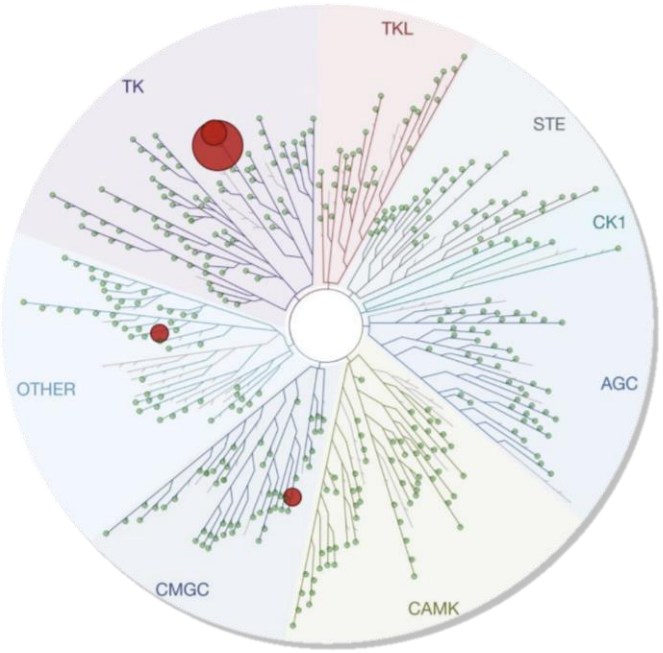
출처: AACR2022

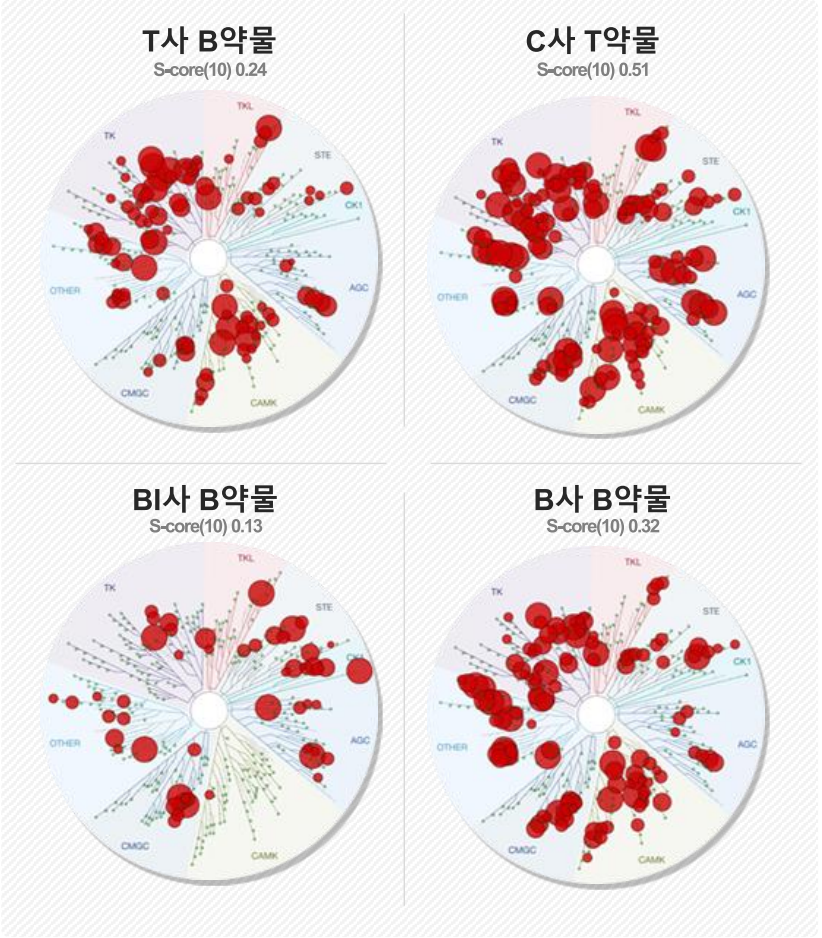
VRN11. Selectivity

현재 EGFR C797S에 대한 치료제가 부재한 가운데, 경쟁 약물 대비 선택성 압도적 우위
이를 바탕으로 Off-target 부작용이 없는 약물 기대

VRN11

S-core(10) = 0.01

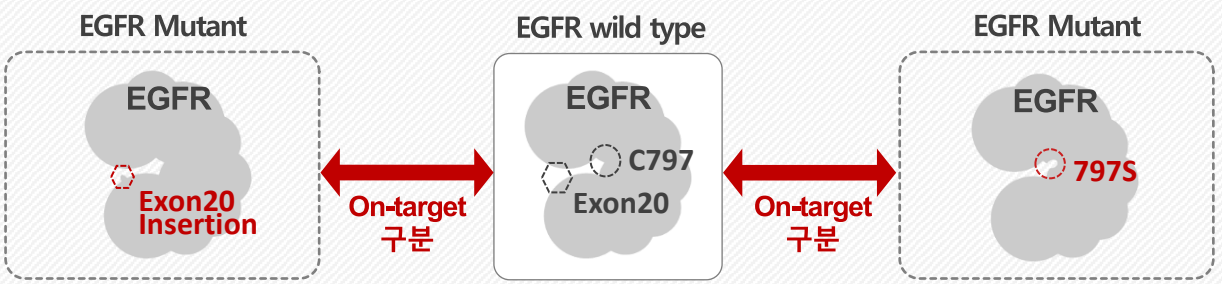




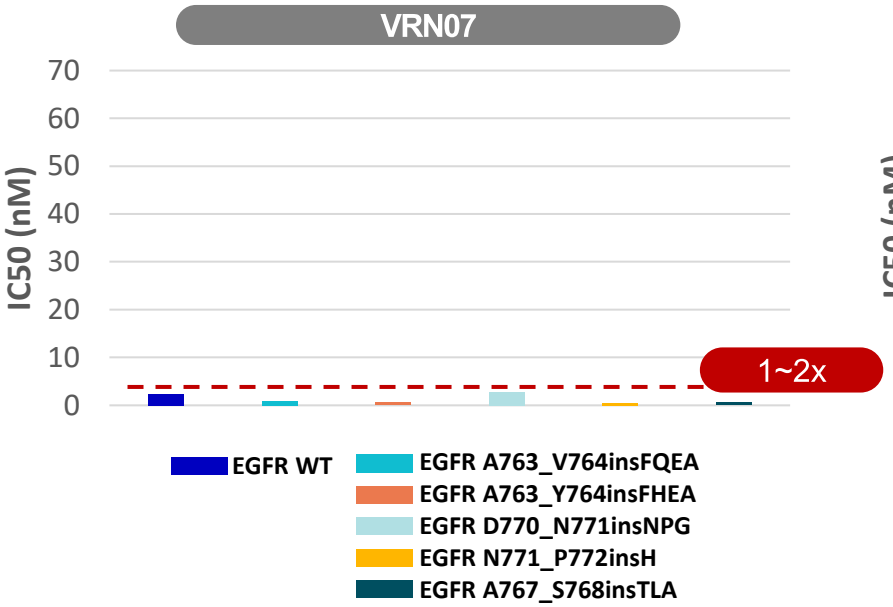
출처: Eurofins DiscoverX Kinomescan, 1 uM concentration

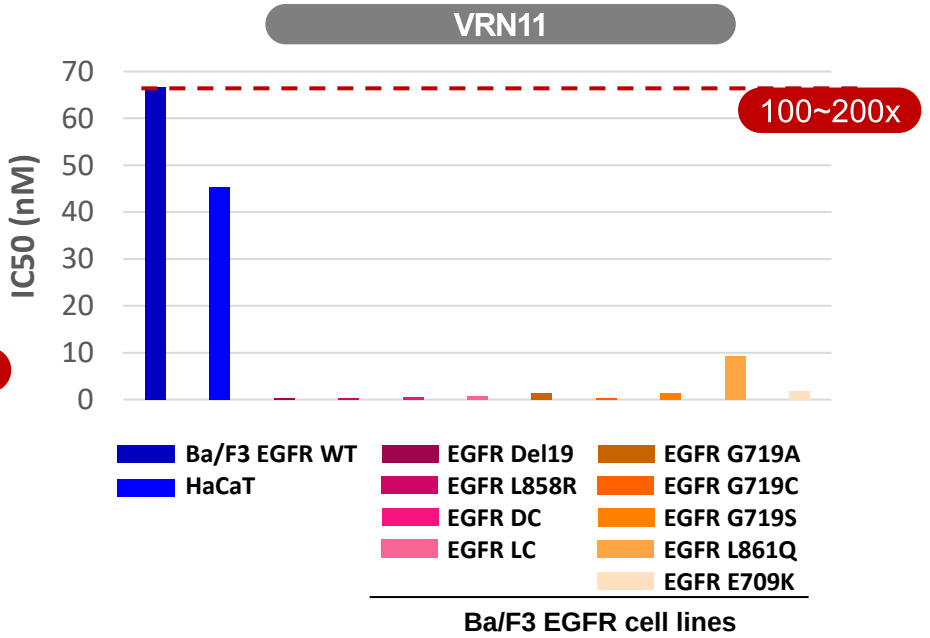
VRN07 & VRN11. On-target WT EGFR sparing

Highly potent against EGFR mutation



- 표피성장인자수용체(EGFR)를 억제하는 약물로 인해 발생하는 EGFR 관련 부작용(피부발진, 여드름양 발진, 손발톱주위염, 설사 등)





출처: AACR-NCI-EORTC, WCLC2023

VRN07 & VRN11. Toxicity

VRN11, On-target/Off-target 부작용이 확인되지 않을 것으로 기대

Clinical trial. On-target Toxicity data

EGFR 구분	약물명	Grade ≥3 부작용	
		Total(%)	On-target Toxicity
Del19 L858R	Tagrisso	34~42% (FLAURA)	Diarrhea(설사) 3%
Del19 L858R	Leclaza	39% (Laser301)	Rash(발진) 1.1%, Diarrhea(설사) 2.3%
Del19 L858R	Laclaza +Rybrevant	75% (MARIPOSA)	<EGFR> Paronychia(손발톱주위염) 11%, Rash(발진) 15%, Diarrhea(설사) 2%, Dermatitis acneiform(여드름양 피부염) 8%, Stomatitis(구내염) 1%, Pruritus(가려움증) 0.5% <MET> Hypoalbuminemia(저알부민혈증) 5%, Peripheral edema(말초 부종) 2%
Exon20 Ins.	Sunvozertinib	39%	Diarrhea(설사) 8%, Rash(발진) 1%, Paronychia(손발톱주위염) 2%
EGFR C797S	BDTX-1535	50%*	Diarrhea(설사) <20%, Rash(발진) <20%, Stomatitis(구내염) <5%, Paronychia(손발톱주위염) <5%
Exon20 Ins.	ORIC-114 (VRN07)	19%*	Diarrhea(설사) 9% , Stomatitis(구내염), 3%, Pruritis(가려움증) 3%
EGFR C797S	VRN11		

출처: ESMO2023, ASCO2023, AACR-NCI-EORTC2023, Ramalingam SS, et al.; FLAURA Investigators. N Engl J Med. 2020 Jan 2;382(1):41-50. doi: 10.1056/NEJMoa1913662. Epub 2019 Nov 21.
*유효 용량 이상의 부작용 데이터

VRN11. NSCLC 시장규모

비소세포폐암 분야에서 돌연변이별 수 조원의 시장 규모 형성

비소세포폐암의 돌연변이별 환자 수 구분(%)

유럽, 미국 대비 동북아 3개국(한,중,일)의 EGFR 돌연변이 발생률이 1.6~2배 이상 높음 (중국 48%, 일본 45%, 한국 43% - 미국 26%, 유럽 15%)

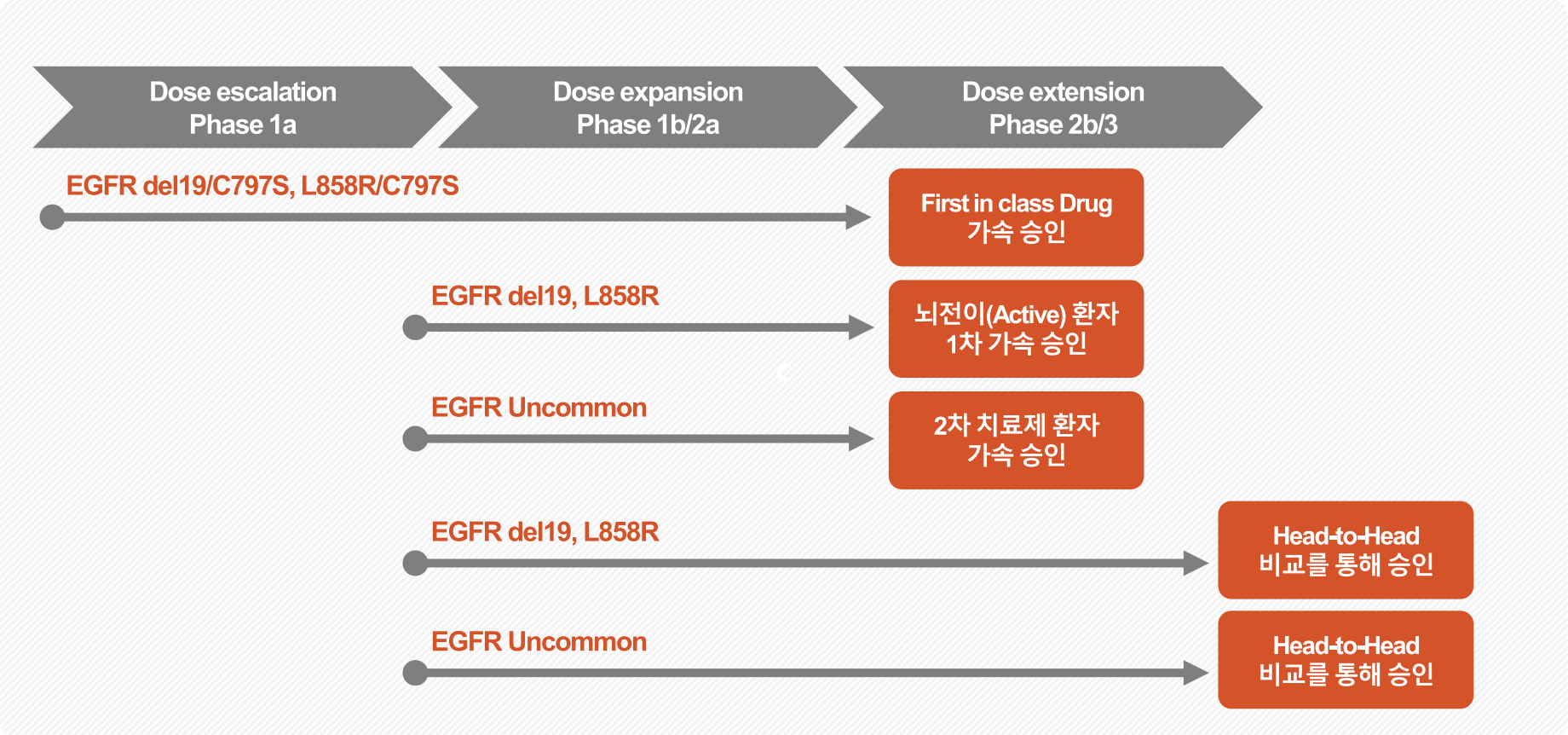
비소세포폐암의 돌연변이별 약물 시장가치 및 매출 추정치

Target Mutant	EGFR C797S	EGFR Exon20 ins.	RET fusion	ROS1
대표 약물명 (기업)	현재 치료제 부재	Rybrevant(Johnson & Johnson)	Gavreto (Blueprint Medicines) Retevmo (Loxo Oncology)	Rozlytrek (Ignyta) Xalkori (Pfizer)
시장규모 (환자 수 기반 추정)	2.5조원 이상	3조원 이상	1.5조원 이상	1조원 이상
Peak Sales	-	-	0.8조원(E, Gavreto) / 1조원(E, Retevmo)	0.3조원(E) / 0.7조원(`17)
Reference Deal	Blueprint Medicines → Zai Lab 전임상 단계, 중국 판권 기술이전 약 7,300억원	Blueprint Medicines-Lengo Therapeutics 전임상 단계, 기업인수 약 5,300억원	Blueprint Medicines → Roche 임상2상, (중국제외) 기술이전 약 2조원 Eli Lilly-Loxo Oncology 임상2상, 기업인수 약 9조원	Ignyta-Roche 임상2상, 약 2조원 기업인수 Turning Point Therapeutic-BMS 임상1/2상, 약 5.1조원 기업인수
개발사	Blueprint Medicines Chia Tai Tianqing Pharmaceutical Group	Takeda Blueprint Medicines	Blueprint Medicines Loxo Oncology	BMS Roche

출처 : (1) Mol Cancer Ther. 2013 Feb;12(2):220-9. doi: 10.1158/1535-7163.MCT-12-0620. Epub 2013 Jan 31. (2) J Hematol Oncol 14, 50 (2021). (3) Clin Cancer Res. 2012 Sep 15;18(18):4910-8. doi: 10.1158/1078-0432.CCR-12-0912. Epub 2012 Jul 3. (4) Mol Cancer. 2018 Feb 19;17(1):29.doi: 10.1186/s12943-018-0778-0.
*EGFR Frequency: Am J Cancer Res. 2015 Aug 15;5(9):2892-911. eCollection 2015 *KRAS Frequency: Cancer Treat Rev.2021 May;96:102179. doi: 10.1016/j.ctrv.2021.102179. Epub 2021 Mar 19 *ROS1 Frequency: J Clin Oncol. 2015;33(9):992-999. doi:10.1200/JCO.2014.58.3302
- Peak Sales: Globaldata, $1 = ₩1,247(서울외국환중개 2023년 1월 일일 매매기준율 평균

VRN11. Planned Next Steps

EGFR 돌연변이 치료제에 존재하는 다양한 환자군에 진입 예정



한국 임상 1상 IND 승인 이후,
- 대만, 1a/1b IND 제출 및 승인 완료
- 향후 미국 임상 IND 제출 예정

EGFR 획득내성 폐암, EGFR 원발성 폐암, EGFR 뇌전이 폐암 등
다양한 EGFR 분야의 치료옵션 기대

Creating Novel Therapeutics
By People With Excellent Expertise
In Drug Design

VORONOI

Thank You