HLB

Human Life Better

August 2024

Intro

Approval Rate vs. Risk

ONE Product Risk

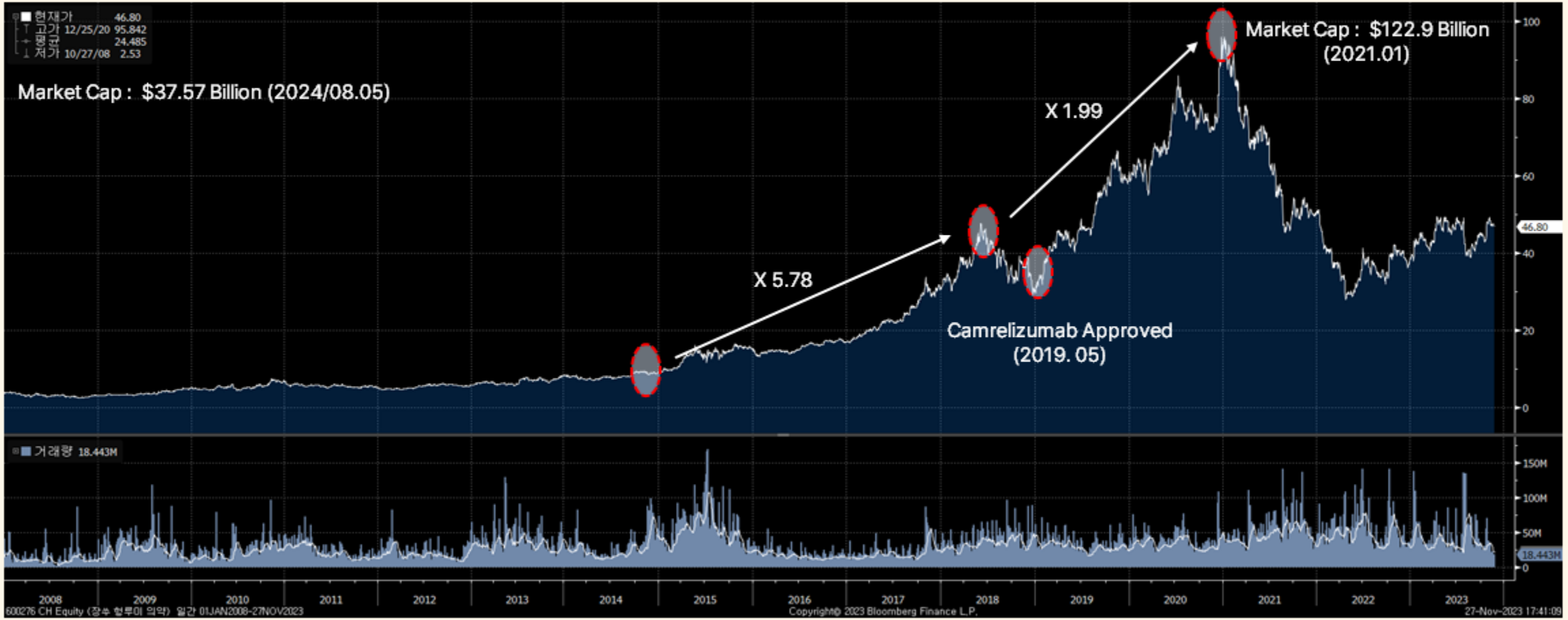
Oncology vs. Semiconductor

	2023	2027
Oncology	$ 300B	$ 500B
Semoconductor	$ 700B	$ 1,000B

HLB Case...

UPSIDE >> RISK

Stock Trend of Hengrui Pharmaceutical



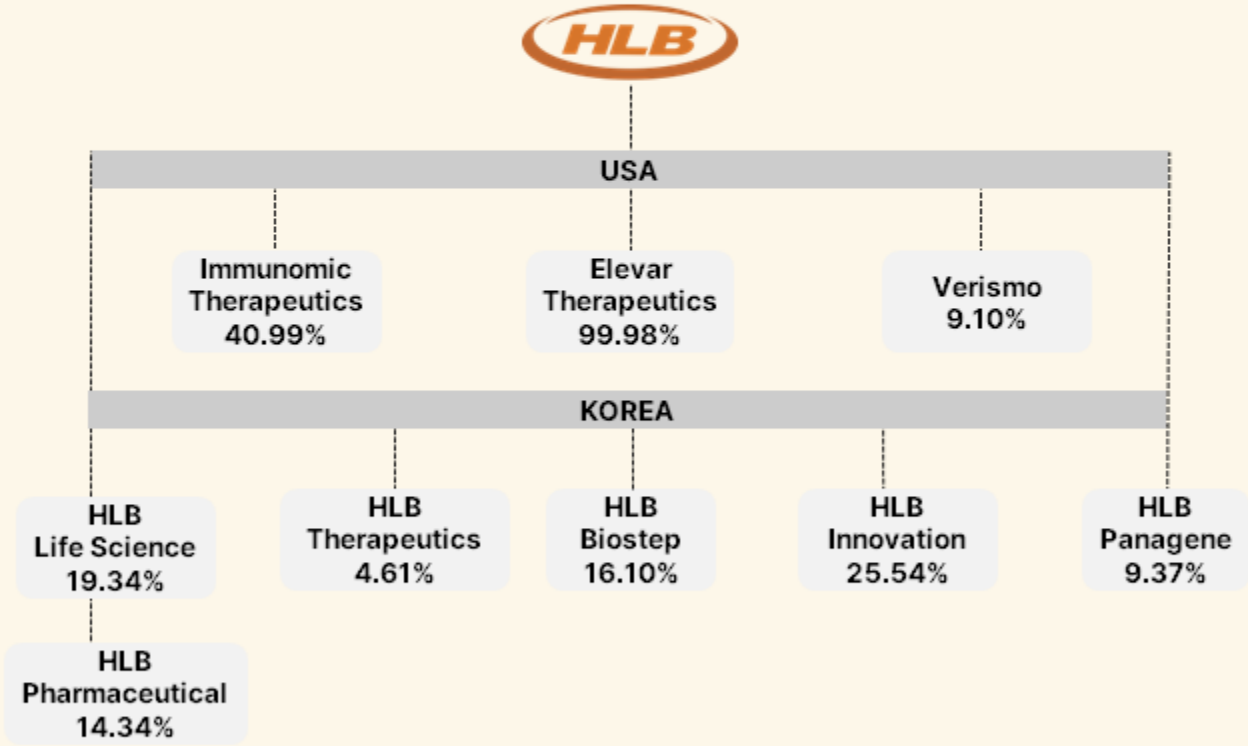
Overview

Company Profile

Unit: USD million

Chairman	Jin Yang Gon
CEO	Jin Yang Gon, Baek Yoon Ki
R&D	182
Business	Bio, Healthcare
Capital (2024. 03)	$471.5
Asset (2024. 03)	$624.1
Liabilities (2024. 03)	$152.6
Ratio of Liabilities (2024.03)	24.5%
Market Cap (2024.08.01)	$8,174

Key Subsidiaries



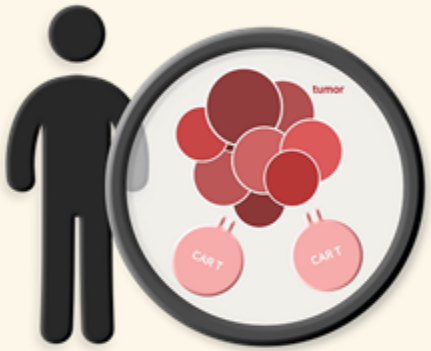
Source:2024 1Q Report $1 USD=1,368.66 KRW by 24/08/01

Pipelines

Company	Indication	Rights	Mono/Combo	Progress of Clinical Development
				Preclinical / Phase 1 / Phase 2 / Phase 3 / NDA
Elevar Therapeutics	HCC 1st line	Global (Ex. China)	Rivoceranib + Camrelizumab	
	ACC 1st line		Rivoceranib	
	GC 3rd/4th line		Rivoceranib	
	GC 2nd line		Paclitaxel Combo	
	Colorectal Cancer 3rd line		Lonsurf Combo	
Immunomic Therapeutics	GBM (ITI-1000)	Global	Dendritic Cell vaccine	
	GBM (ITI-1001)		DNA vaccine	
	Merkel Cell Carcinoma (ITI-3000)		DNA vaccine	
Verismo Therapeutics	Solid Cancer (SynKIR-110)	Global	CAR-T Therapy	
HLB Therapeutics	Dry Eye Syndrome	Global	RGN-259	
	Neurotrophic Keratitis			

*HCC=Hepatocellular Carcinoma, ACC=Adenoid Cystic Carcinoma, GC=Gastric Cancer, GBM=Glioblasoma

Future Pipeline of HLB Group



CAR-T

Long-Acting Injection (LAI)

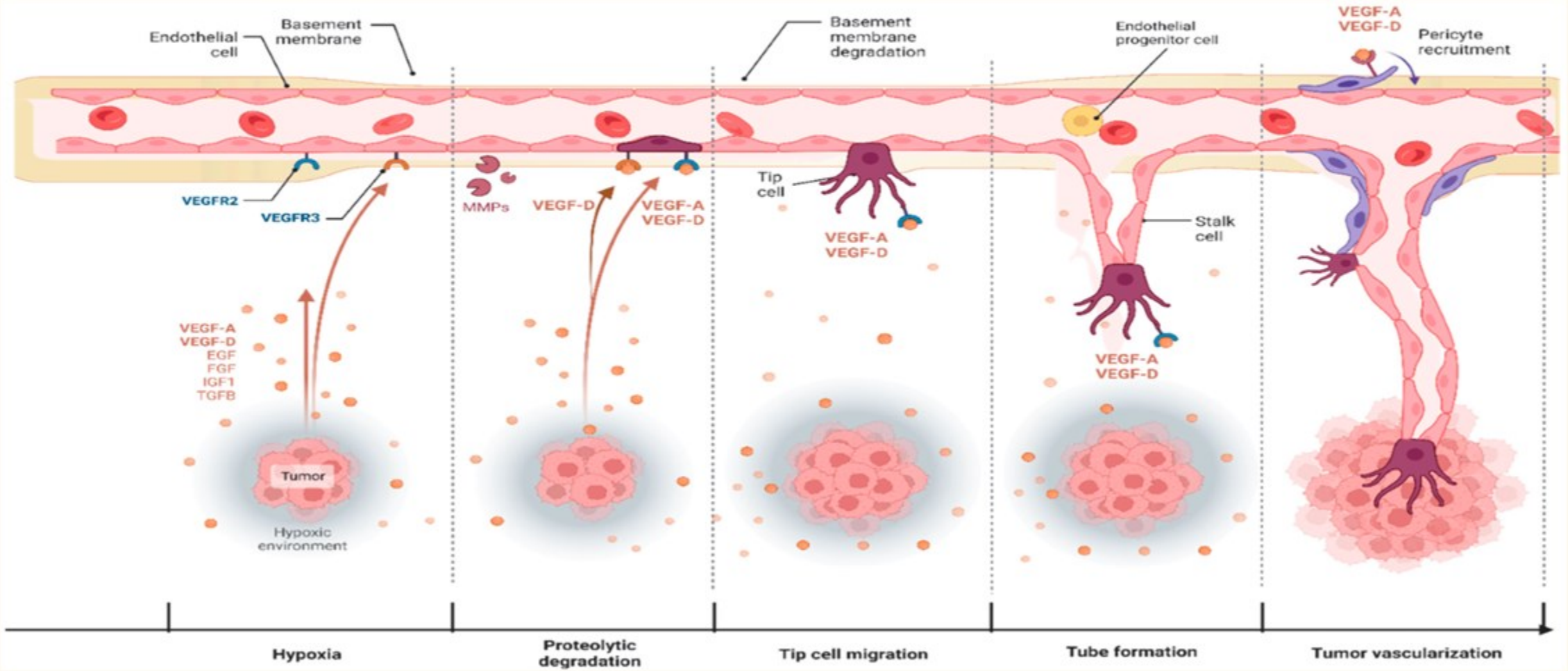
AI Drug Development (400 Billion Data)

HCC 1st Line Market Players

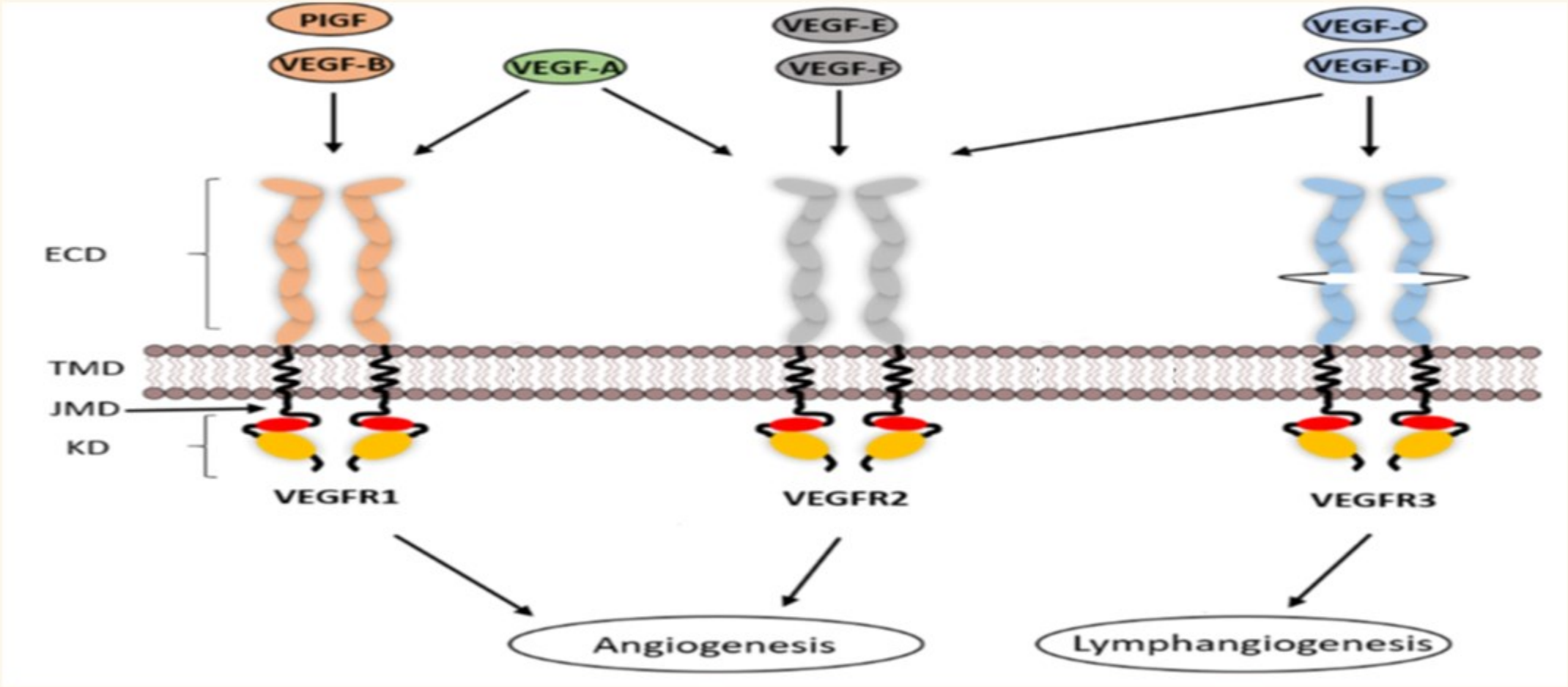
Therapy	Rivoceranib + Camrelizumab	Atezolizumab + Bevacizumab	Tremelimumab + Durvalumab	Lenvatinib	Sorafenib
Patients	**543**	501	782	954	602
Control Group	**Sorafenib**	Sorafenib	Sorafenib	Sorafenib (Inequality)	Placebo
OS	**23.8 vs. 15.2 HR 0.62**	19.2 vs 13.4 HR 0.66	16.4 vs 13.8 HR 0.78	13.6 vs 12.3 HR: 0.92	10.7 vs 7.9 HR: 0.69
PFS	**5.6 vs. 3.7 HR 0.52**	6.8 vs 4.3 HR 0.59	3.8 vs 4.1 HR 0.9	7.4 vs 3.7 HR: 0.66	5.5 vs 2.8
ORR	**25.4% vs. 5.9%**	27.3% vs 11.9%	20.1% vs 5.1%	18.8% vs 6.5%	2% vs 1%
DCR	**78.3% vs. 53.9%**		73.6% vs. 55.3%		43% vs 32%
Market Share	**Target 50%**	52%	25%		
Approval	***CRL Issued**	2020	2022	2018	2007

Source: Clinical Trail Gov.
*May 2023 NDA Filing → July NDA Submission → May 16, CRL Issued

Angiogenesis



Mechanism of Action of Angiogenesis



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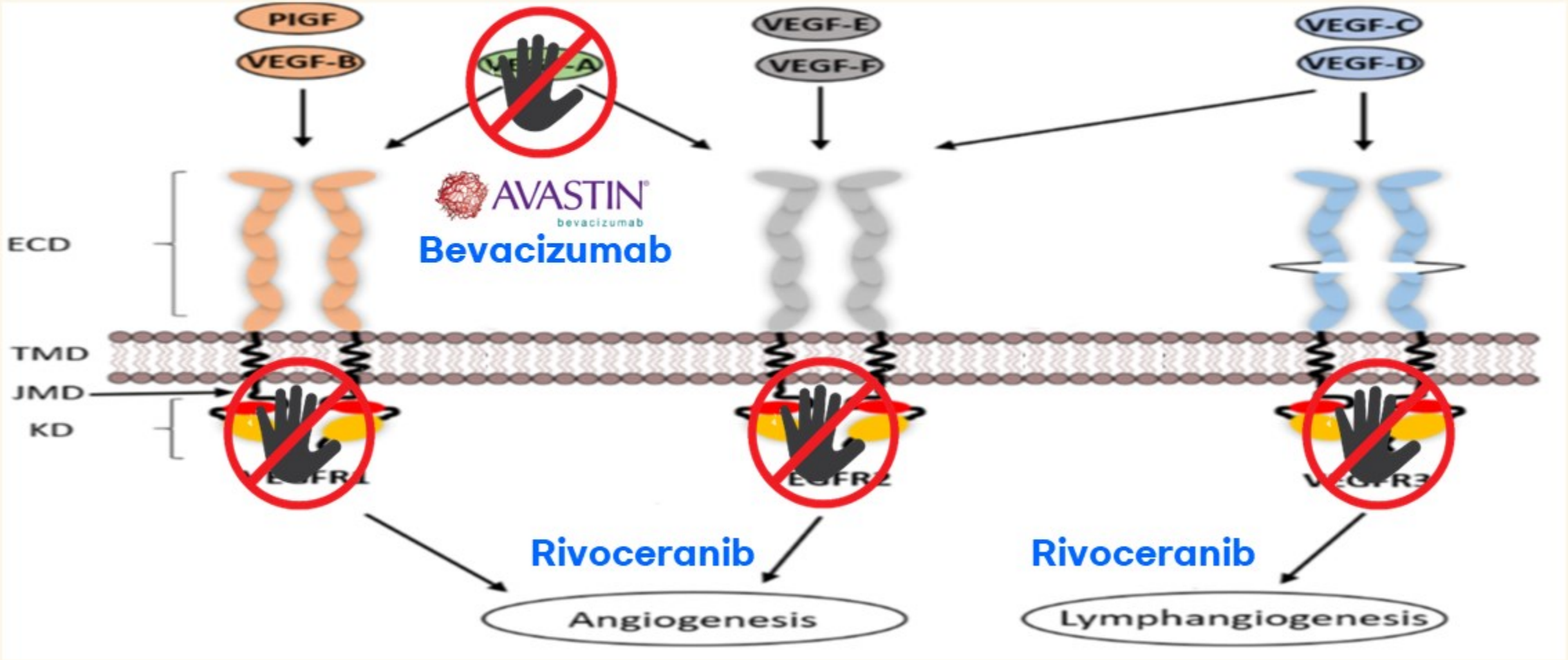
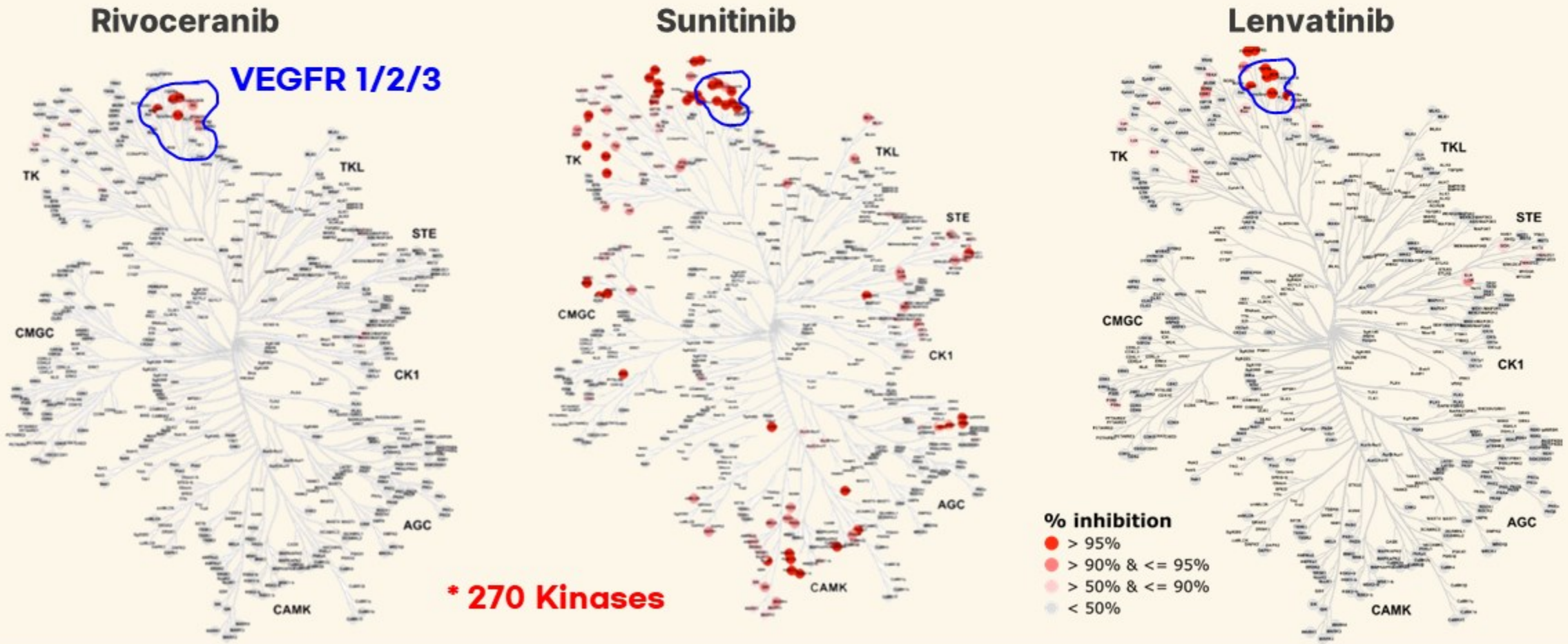


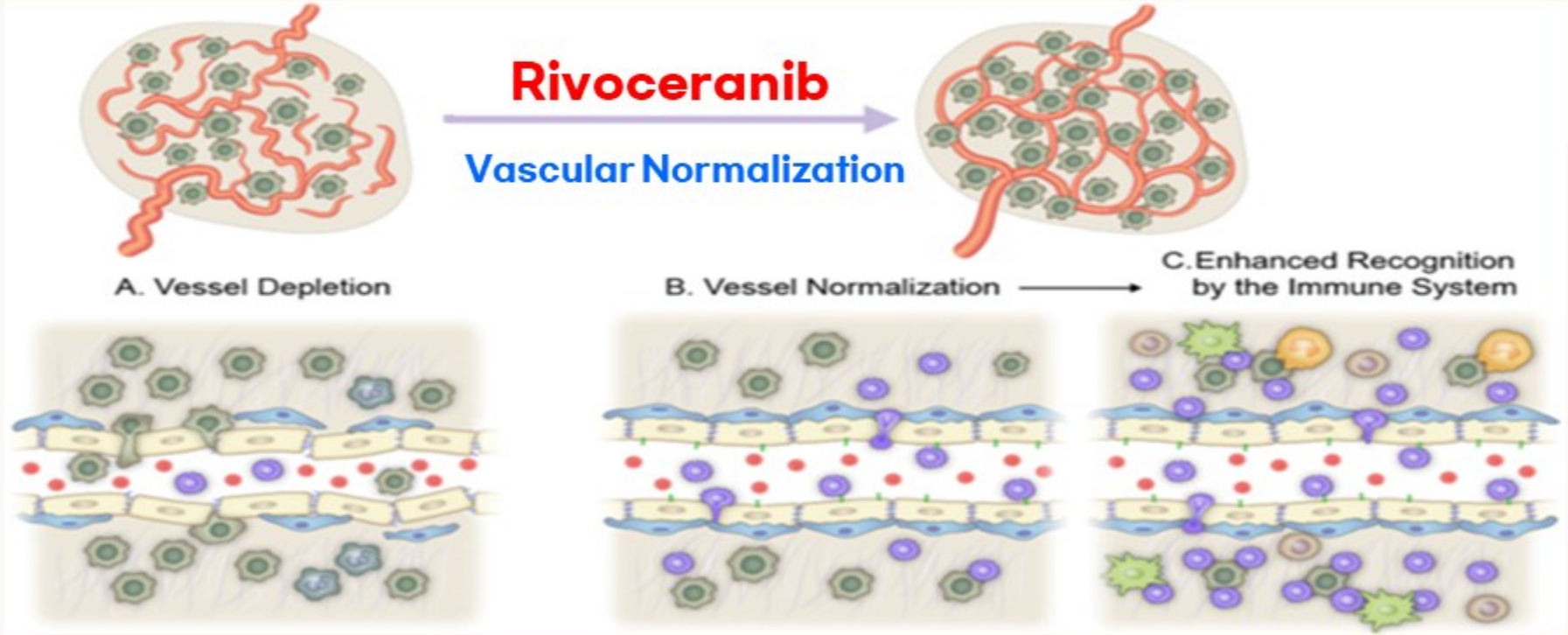
Rivoceranib: Highly Selective VEGFR Inhibitor



* 270 Kinases

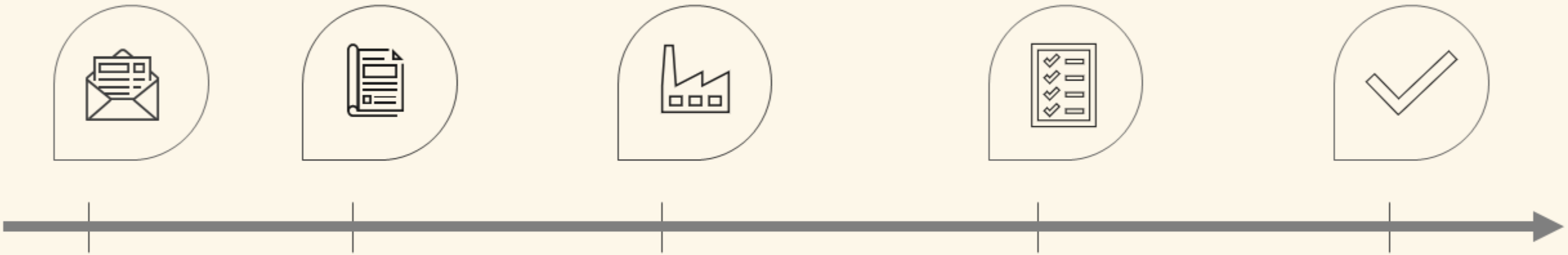
Source: Cancer Chemotherapy and Pharmacology (2023) 91:491–499

Rivoceranib: Mechanism of Action



Inhibits Angiogenesis → Vascular Normalization → Increase T Cell infiltration → Suppress Cancer

Status of NDA Review



2023. 5
- NDA Submission

2023.7
- NDA Review Filed

2023. 11/12
- Completed FDA Mid-Cycle Review
- **Completed CMC for Rivoceranib/Camrelizumab**

2024. 3
- Completed FDA Late-Cycle Review

2024. 5
- **CRL Issued**

Status of Update After CRL Issue

2023. 12

- Received 10 inquiries related to CMC

2024. 2/3

- Submitted responses related to CMC (2 Times)

2024. 5.16

- CRL Issued

2024. 7. 02

- Received PAL, No additional deficiencies noted
- Concluded the TYPE A Meeting
- FDA requested a resubmission

2024. 9

- Plan to resubmit the NDA
- Plan to submit updated 23.8 months OS data

2025. 3

If Class 2 Expected Timeline for the Result

OR

2024. 11

If Class 1 Expected Timeline for the Result

Merck & Daiichi Sankyo CRL Issue Case

Daiichi-Sankyo MERCK

News Release

Patritumab Deruxtecan BLA Submission Receives Complete Response Letter from FDA Due to Inspection Findings at Third-Party Manufacturer

The letter did not identify any issues with the efficacy or safety data submitted in the application

BASKING RIDGE, N.J. & RAHWAY, N.J., June 26, 2024 – The U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) for the Biologics License Application (BLA) seeking accelerated approval of Daiichi Sankyo (TSE: 4568) and Merck's (known as MSD outside of the United States and Canada) (NYSE: MRK) patritumab deruxtecan (HER3-DXd) for the treatment of adult patients with locally advanced or metastatic EGFR-mutated non-small cell lung cancer (NSCLC) previously treated with two or more systemic therapies.

The CRL results from findings pertaining to an inspection of a third-party manufacturing facility. The CRL did not identify any issues with the efficacy or safety data submitted.

CRL

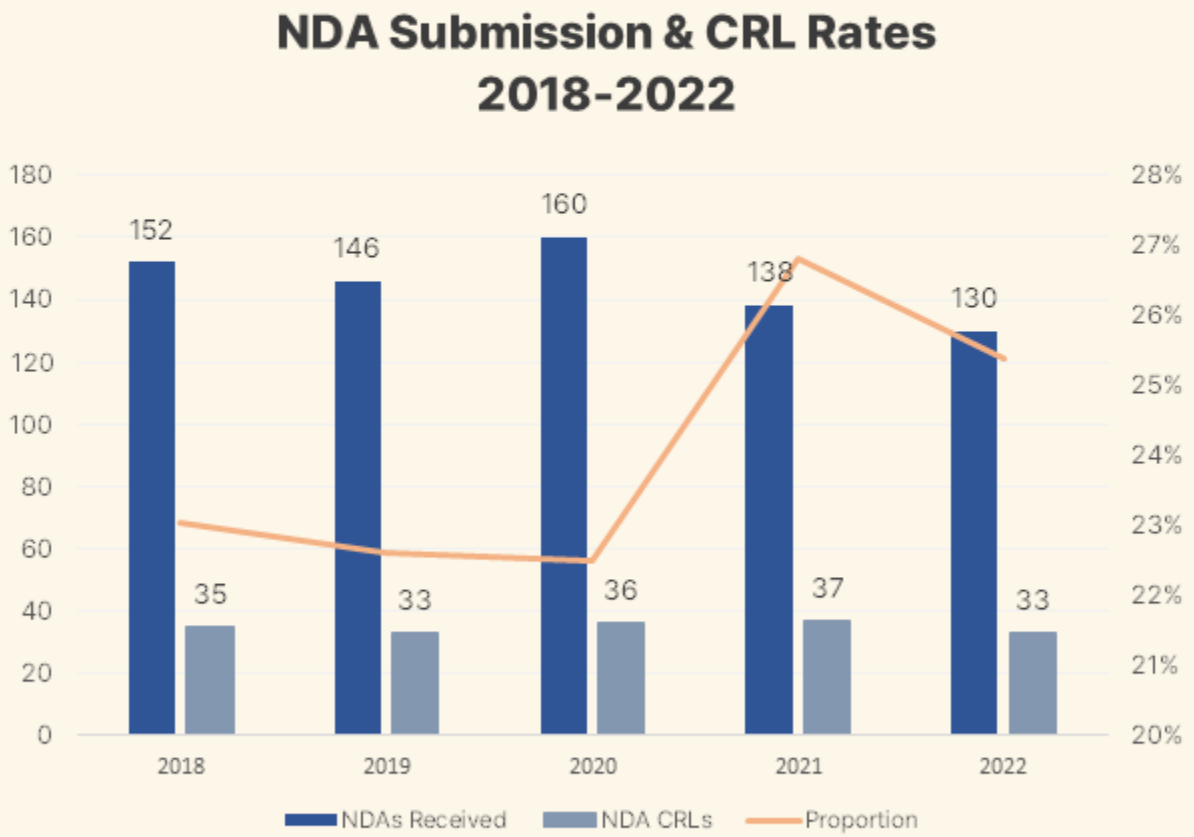
On 6/26, 2024, Merck and Daiichi Sankyo Received a CRL for the BLA Submission of Patritumab Deruxtecan

'Facility'

Received a CRL Letter Due to 'Facility Issues' ; Preparing for Resubmission Based on FDA Feedback (Same case with HLB)

Source: MERCK

CRL Trends



24%

Average CRL Rates for NDA Submission (Past 5 years)

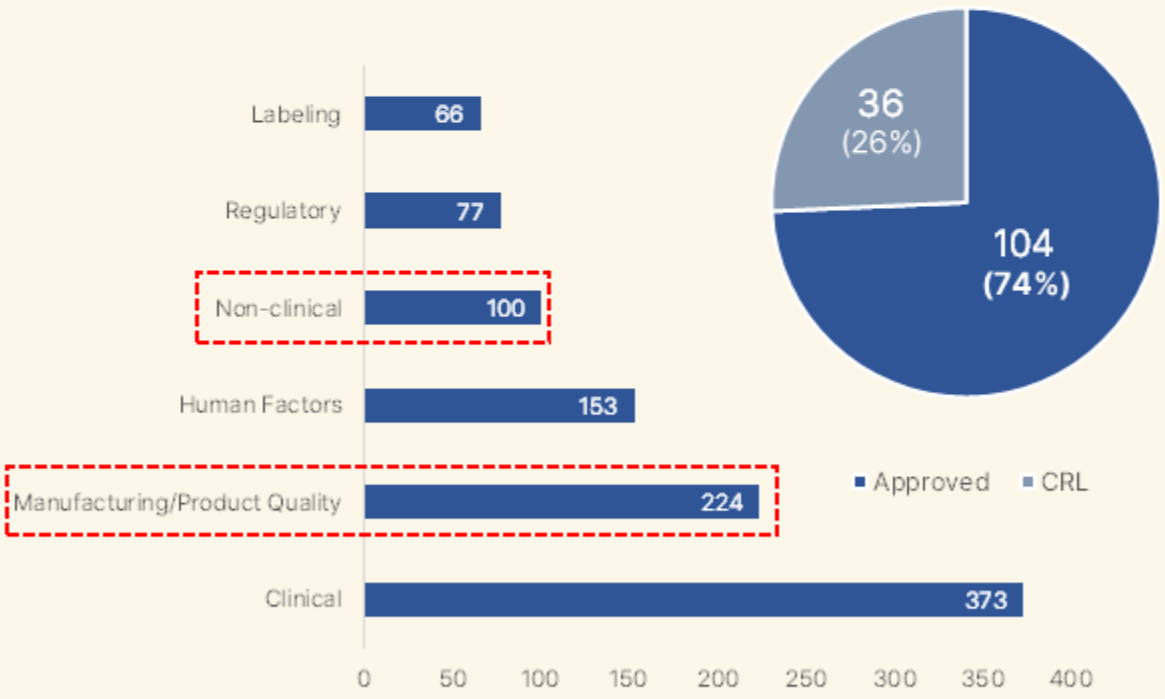
89%

Related to CMC Issues is the highest approval rate among all CRL issues
(Only 24% approved for Clinical Deficiencies)

Source: WELLS FARGO Research, FDA CRL Deep Dive, June 6, 2024

CRL Trends

Time to Resubmission & Approval Rates by CRL Types



100~224 Days

Estimated Time to Resubmission for HLB (Nonclinical or Manufacturing)

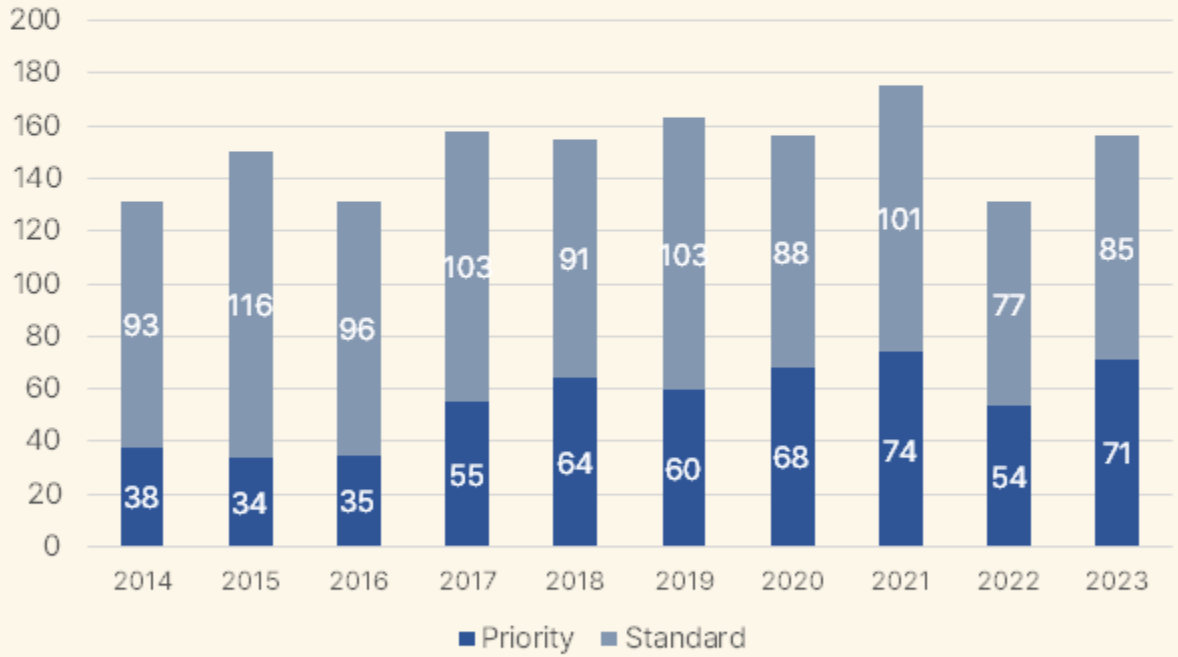
74%

Approval Rates After CRLs (Only 26% Rejected or Received Another CRL issues)

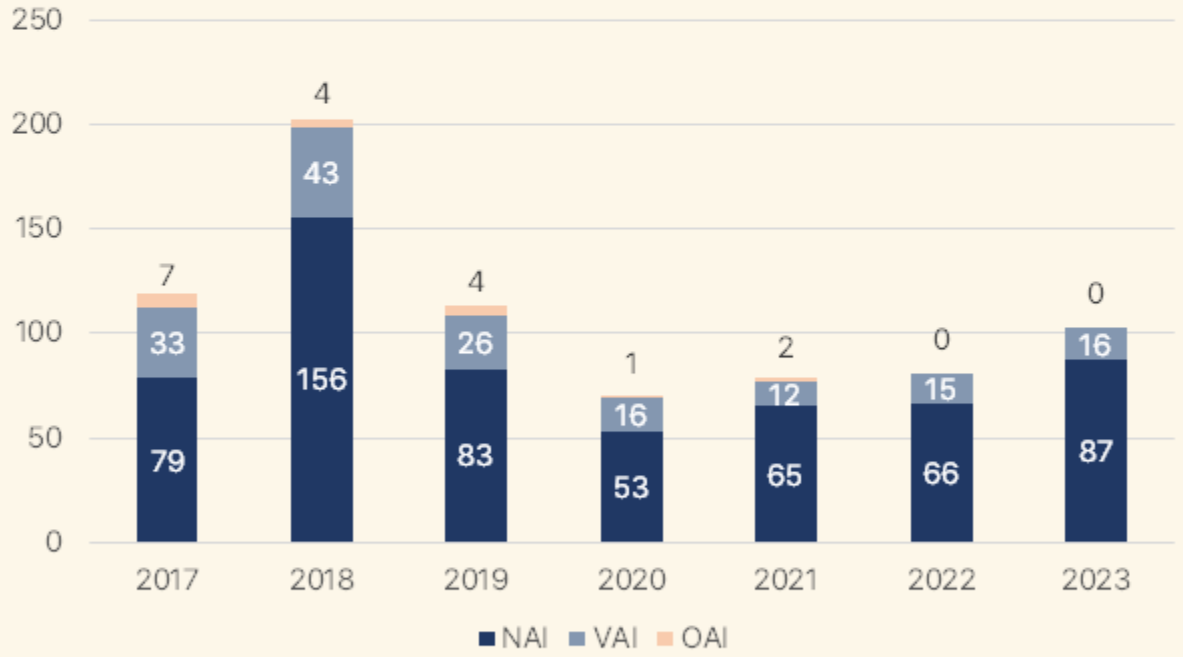
Source: WELLS FARGO Research, FDA CRL Deep Dive, June 6, 2024

PUDFA Trend Graphs

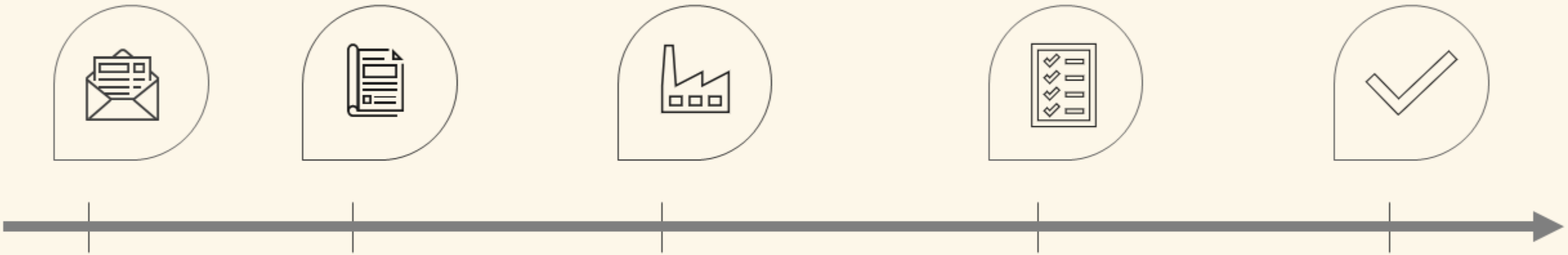
Number of FDA NDA Submission



BIMO Inspection



Status of NDA Review



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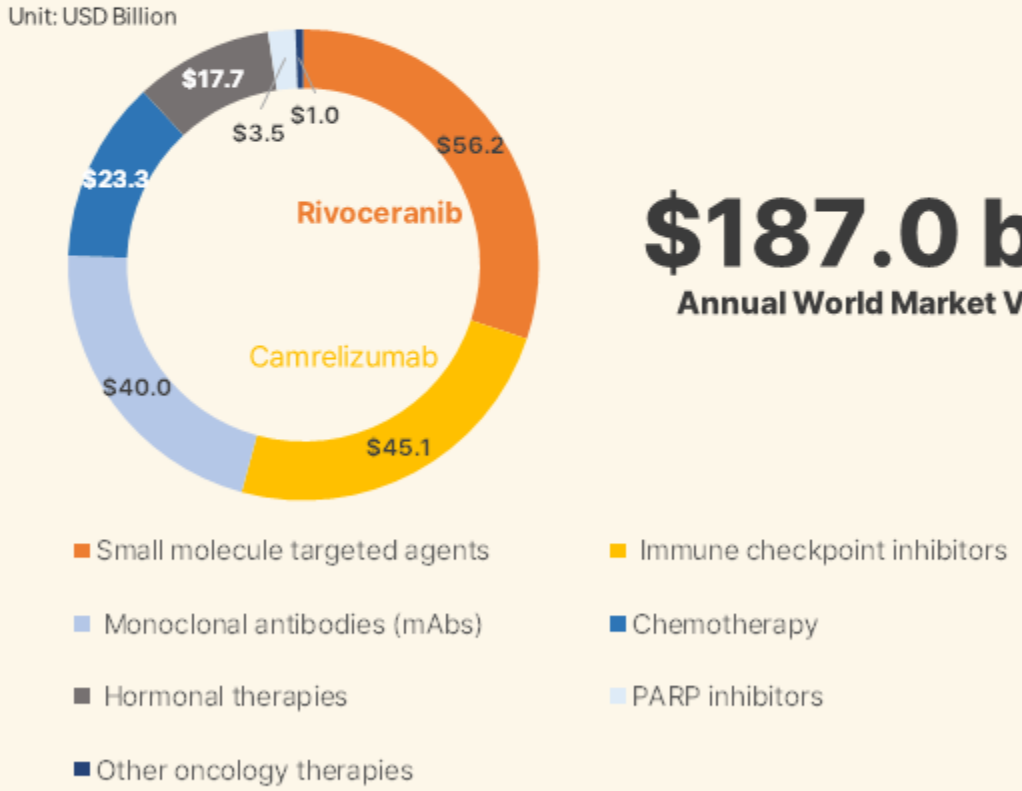
Comparison & Analysis of Updated Data

Rivoceranib+Camrelizumab vs. Nivolumab+Ipilimumab

	Experimental	Control	Experimental	Control	Note
	Rivo+Cam	Sorafenib	Nivo+Ipl	LEN/SOR	
mOS	23.8	15.2	23.7	20.6	
ORR	25.4	5.9	36	13	331% vs. 177%
TRAE	24.3%		41%		
HR (95% CI); p valule	0.64		0.79		FDA Approval Criteria 0.8

Global Oncology Market Value

Therapy Area Global Market



$187.0 bn

Annual World Market Value

Unmet Medical Need & Global Market

2nd

Cancer is the Second leading Cause of death worldwide.

16.3m

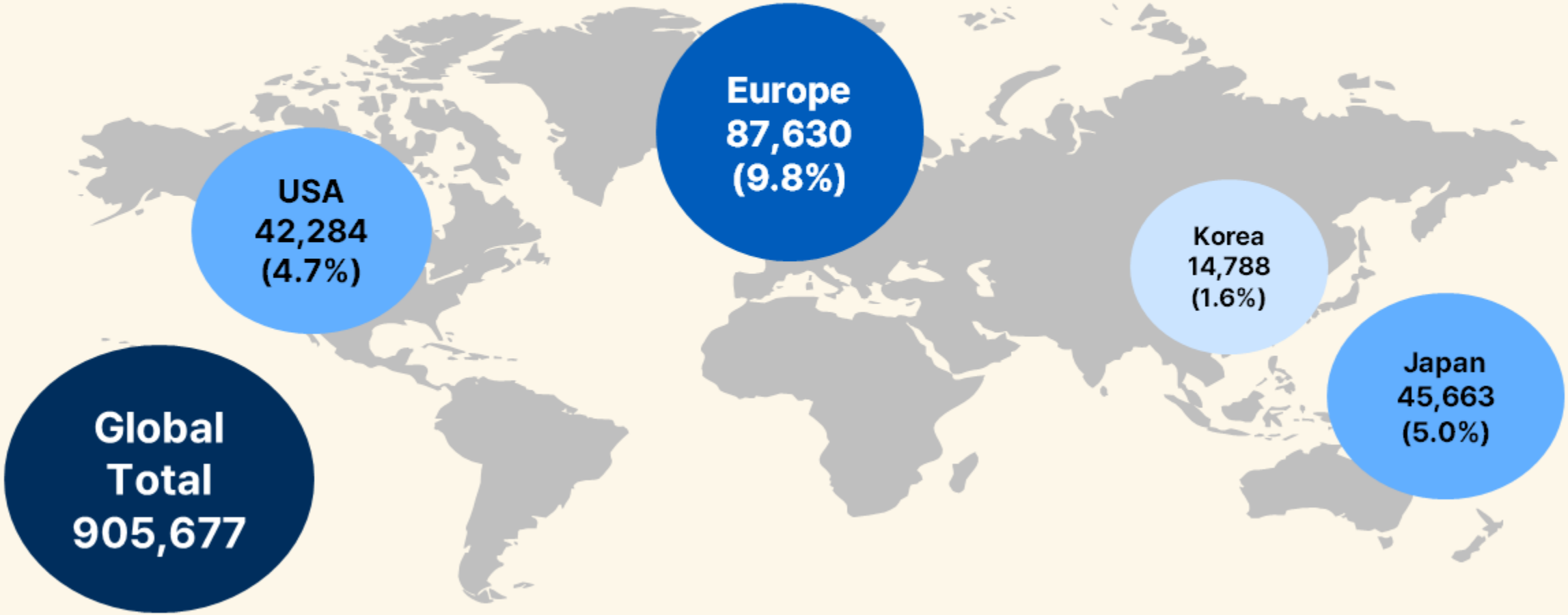
By 2040, cancer is expected to account for 16.3 million deaths annually across the globe

Source: IQVIA

Rivoceranib: Revenue Structure

$$\text{Revenue} = f\left(\frac{\text{\# of Patients}}{\text{HCC Patients}} \text{ X Dosage Period X Drug Price X Market Shares}\right)$$

Global Liver Cancer Patients Data



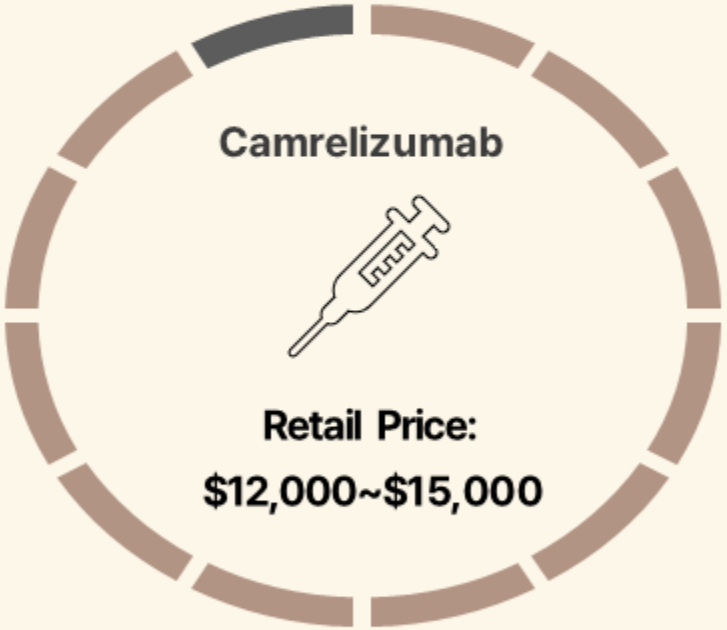
Source: WHO, American Cancer Society, World Cancer Research Fund International, Digestive Cancers Europe, Clinical & Molecular Hepatology

Sales Profit Margin

COGS :
$144.84/month

Gross Profit Margin 99.28%

COGS :
$220.68/month



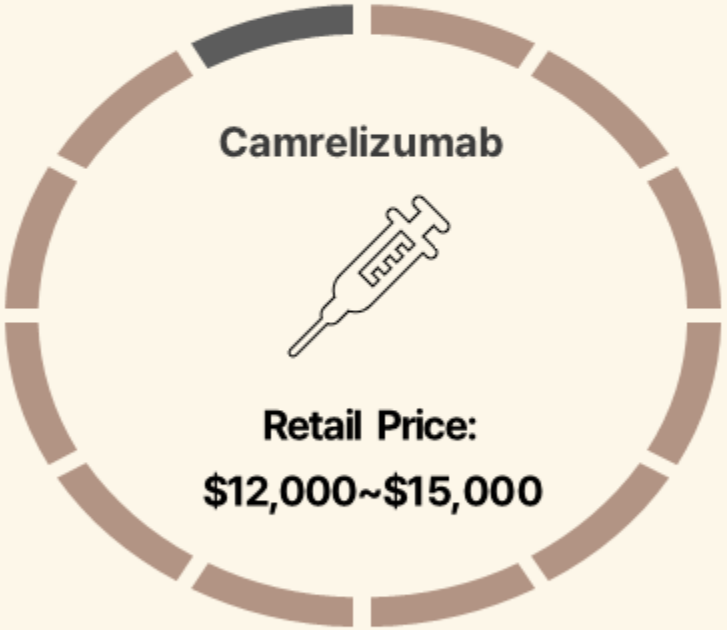
Gross Profit Margin 98.16%

Operating Profit Margin

COGS :
$144.84/month

Profit Margin Rate 87.0%

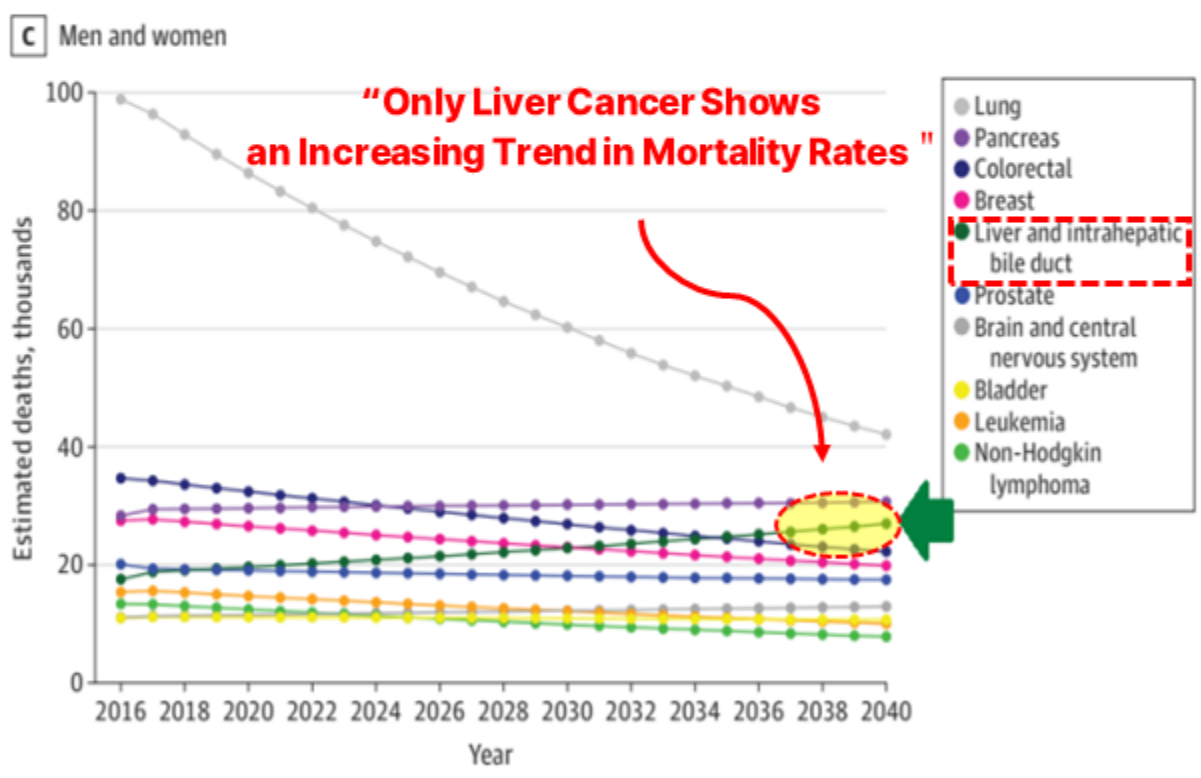
COGS :
$220.68/month



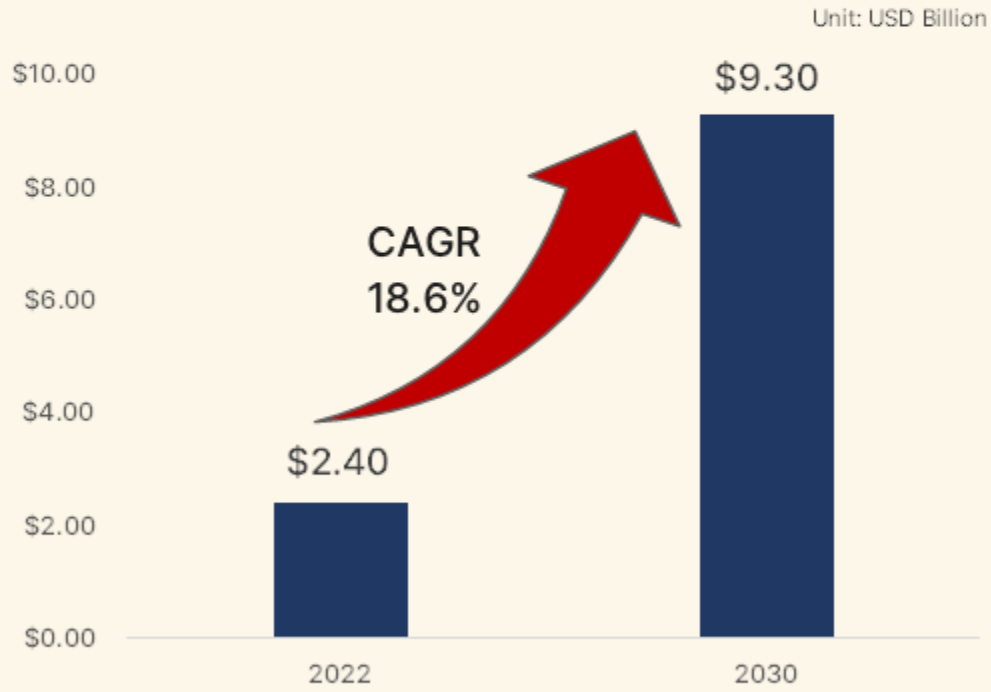
Profit Margin Rate 57.5%

Market Growth of Liver Cancer

Trends in Cancer-Specific Mortality Rates



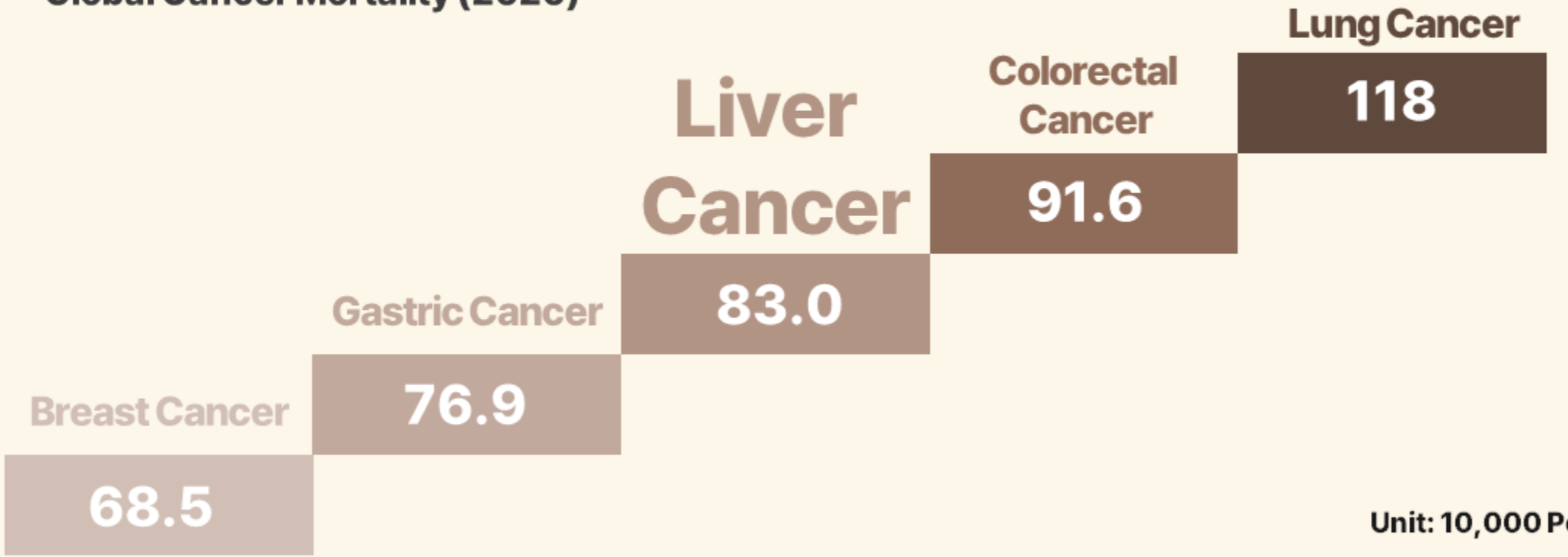
Global Liver Cancer Market Size



Source: Global Liver Cancer Drugs Strategic Market Report to 2030 by Yahoo finance, Feb. 11, 2023

Global Liver Cancer Statistics

Global Cancer Mortality (2020)

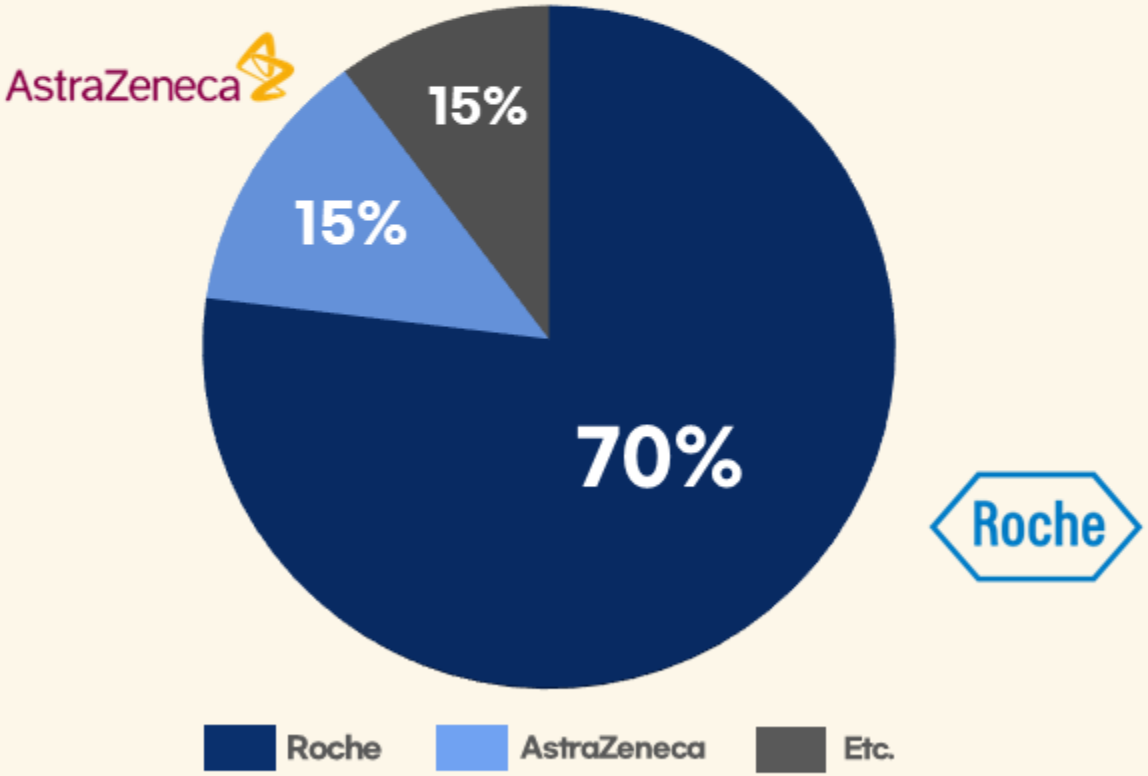


Unit: 10,000 People

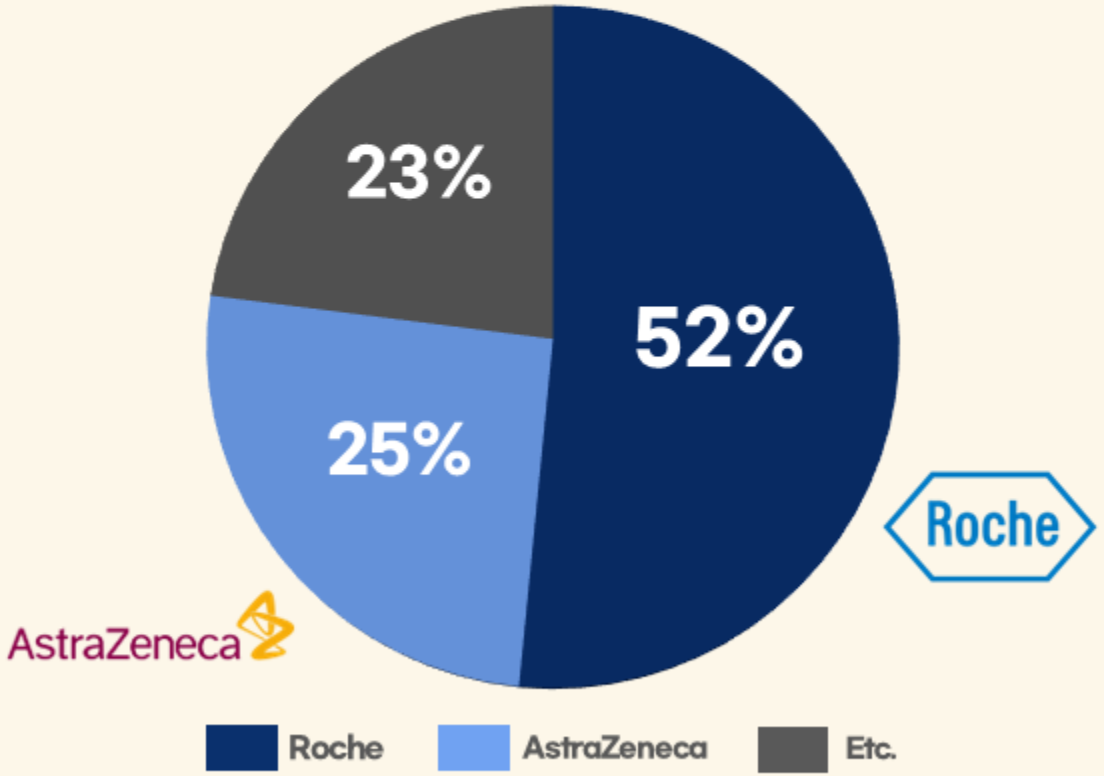
Source: WHO Cancer Statistic

Key Players of Market Share in HCC 1st Line

As of the end of February 2023



As of the end of November 2023



Source: ElevarTx HCC Market Overview BrandImpact by IQVIA Oct, 2023

Key Player's Revenue After NDA Approval

Unit: USD Million

Company	Drug	Revenue ($)					
		2018	2019	2020	2021	2022	2023
Roche	Avastin			5,319	3,343	2,321	1,757
	Tecentriq			2,919	4,326	3,894	4,206
AstraZeneca	Imfinzi					*2,784	*4,237
	Imjudo						
Eisai	Lenvima	390	697	834	1,198	1,555	1,854
		2009	2010	2011	2012		
Bayer	Sorafenib	117.69	115.53	151.78	217.5		

As the 2022, 2023 Annual Report of AstraZeneca, it is specified that the sales of Imjudo are included in the Imfinzi revenue.

Source: Bloomberg, 10K form from each companies

Marketing Points for Commercialization

Longest OS Value
23.8 months

Superior Efficacy

For High-Risk
Bleeding Patients

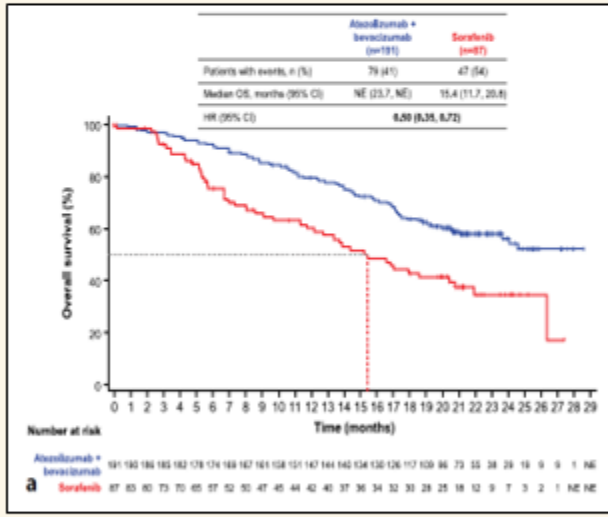
Effective from
All Type of Virus

Marketing Point 1 : Longest Overall Survival

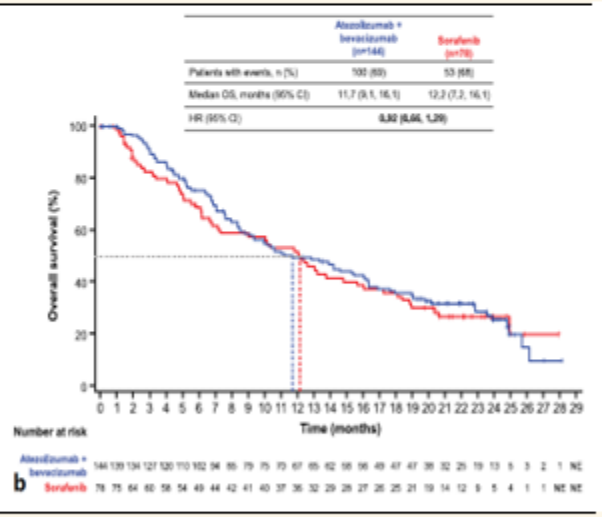
Marketing Points 2 : Superior Efficacy

Imbrave-150 (Roche)
Atezolizumab (Tecentriq) + Bevacizumab (Avastin)

ALBI Grade 1



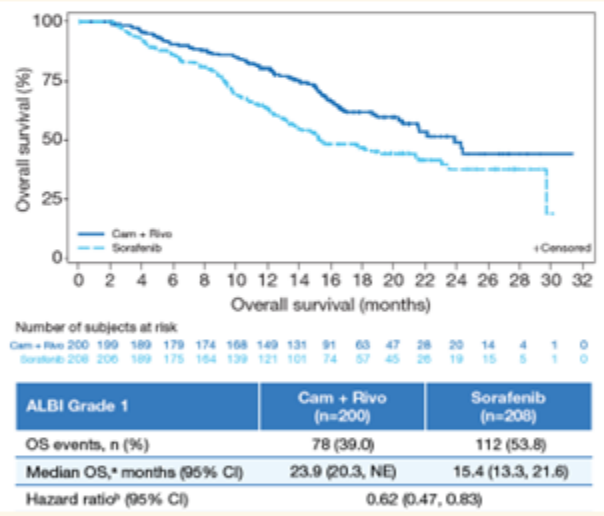
ALBI Grade 2



- ✓ The efficacy favorable only ALBI Grade 1 patients
- ✓ ALBI G1 HR : 0.5 (0.35-0.72), ALBI G2 HR: **0.92 (0.66-1.29)

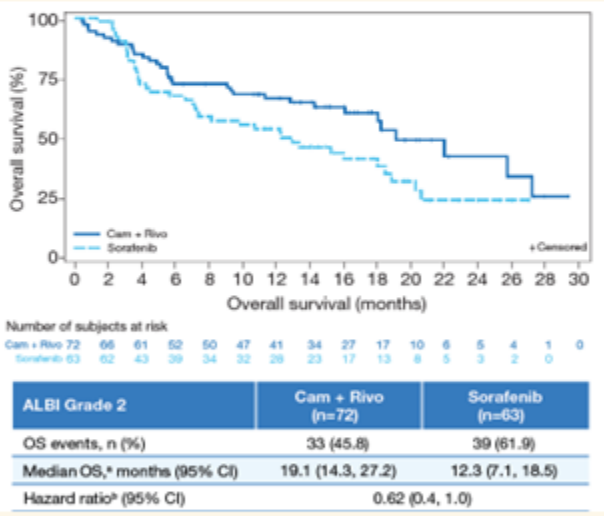
CARES-310 (HLB & Elevar)
Rivoceranib + Camrelizumab

ALBI Grade 1



ALBI Grade 1	Cam + Rivo (n=200)	Sorafenib (n=208)
OS events, n (%)	78 (39.0)	112 (53.8)
Median OS,* months (95% CI)	23.9 (20.3, NE)	15.4 (13.3, 21.6)
Hazard ratio† (95% CI)	0.62 (0.47, 0.83)	

ALBI Grade 2



ALBI Grade 2	Cam + Rivo (n=72)	Sorafenib (n=63)
OS events, n (%)	33 (45.8)	39 (61.9)
Median OS,* months (95% CI)	19.1 (14.3, 27.2)	12.3 (7.1, 18.5)
Hazard ratio† (95% CI)	0.62 (0.4, 1.0)	

- ✓ Favorable for all types of ALBI Grade patients and especially more favorable for ALBI Grade 2 patients than Roche's Products.
- ✓ ALBI G1 HR: 0.62 (0.47-0.83), ALBI G2 HR: 0.62 (0.4-1.0)

Source: Liver Cancer 2023, Supplementary appendix, Lancet 2023; published online July 24.
*ALBI 1/2 Grade is an indicator of the ability of liver function to deteriorate, Grade 2 patients have lower liver function than Grade 1 patients.
**Hazard Ratio (HR) means that the closer to 1.0, the less effective it is.

Marketing Points 3 : For High-Risk Bleeding Patients

Side Effects of Avastin

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use AVASTIN safely and effectively. See full prescribing information for AVASTIN.

AVASTIN® (bevacizumab) injection, for intravenous use
Initial U.S. Approval: 2004

----------RECENT MAJOR CHANGES----------

Indications and Usage, Hepatocellular Carcinoma (1.7)	05/2020
Dosage and Administration, Hepatocellular Carcinoma (2.8)	05/2020
Boxed Warning, Removed	06/2019
Warnings and Precautions (5.3, 5.9)	05/2020

5.3 Hemorrhage

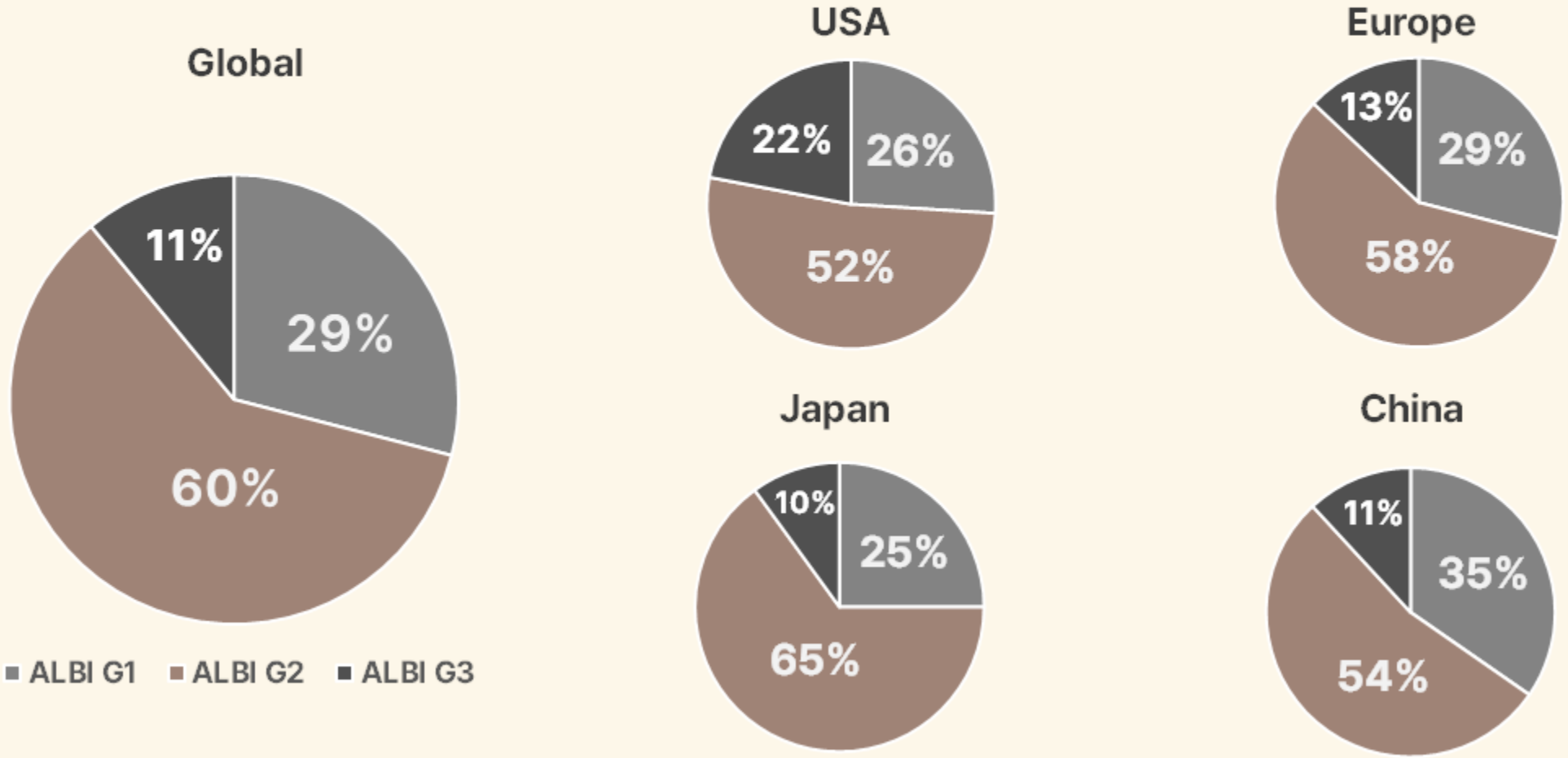
Avastin can result in two distinct patterns of bleeding: minor hemorrhage, which is most commonly Grade 1 epistaxis, and serious hemorrhage, which in some cases has been fatal. Severe or fatal hemorrhage, including hemoptysis, gastrointestinal bleeding, hematemesis, CNS hemorrhage, epistaxis, and vaginal bleeding, occurred up to 5-fold more frequently in patients receiving Avastin compared to patients receiving chemotherapy alone. Across clinical studies, the incidence of Grades 3-5 hemorrhagic events ranged from 0.4% to 7% in patients receiving Avastin *[see Adverse Reactions (6.1)]*.

Controllable Bleeding Side Effects

- ☑ Lower Incidence of Gastrointestinal Bleeding
- ☑ Quick Response to Bleeding Occurrences
  Half Life: Avastin 20 Days vs. Rivoceranib 11 Hrs
- ☑ Prescribable for High-Risk Bleeding Patients

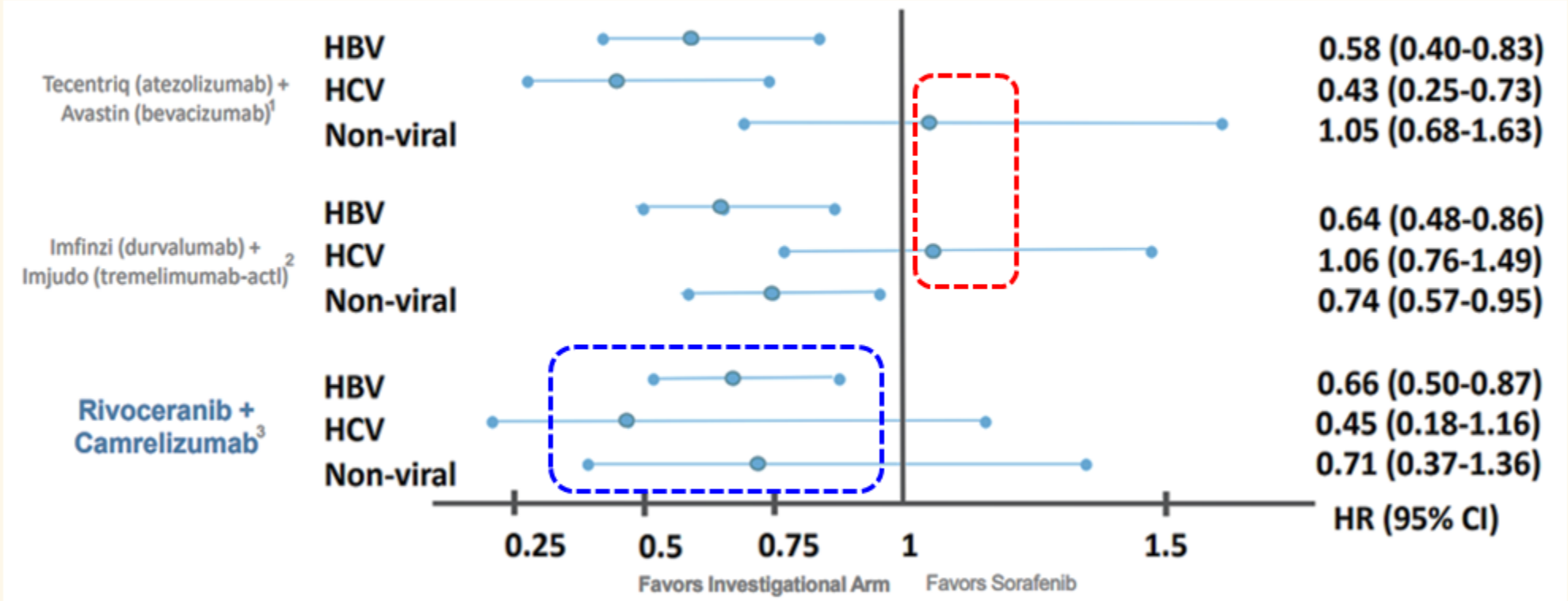
An evaluation for the presence of varices is recommended within 6 months of initiation of Avastin in patients with HCC. There is lack of clinical data to support the safety of Avastin in patients with variceal bleeding within 6 months prior to treatment, untreated or incompletely treated varices with bleeding, or high risk of bleeding because these patients were excluded from clinical trials of Avastin in HCC *[see Clinical Studies (14.10)]*.

Global Patients by ALBI Grade



Source: Karger.com/Albumin-Bilirubin Grade Analyses of Atezolizumab plus Bevacizumab versus Sorafenib in Patients with Unresectable Hepatocellular Carcinoma: A Post Hoc Analysis of the Phase III IMbrave150 Study

Marketing Points 4 : Effective For All Types of Virus



✓ Demonstration as high efficacy across all etiological patient groups among current HCC 1st line therapies.

Best-in-Class Clinical Data

Candidate Drugs for Approval

Company	Drug	NCT #	Clinical Phase	Clinical Trial Completion Period
Junshi Biosciences	Toripalimab	NCT04523493	Phase 3	09.01.2026
AstraZeneca	Durvalumab	NCT03847428	Phase 3	08.31.2025
BMS	Nivolumab+Relatlimab	NCT05337137	Phase 1/2	12.15.2026
BMS	Nivolumab+Ipilimumab	NCT04039607	Phase 3	06.30.2025
Merck	Pembrolizumab	NCT03867084	Phase 3	08.31.2029
LG Chem+AstraZeneca	Tivozanib+Durvalumab	NCT03970616	Phase 1/2	04.04.2023

- ✓ There is **NO** drug currently in clinical trials targeting HCC 1st line treatment that is expected to be commercialized **within the next 5 years.**
- ✓ During this period, it is possible to maximize the sales of Rivoceranib/Camrelizumab and secure a stable market share.

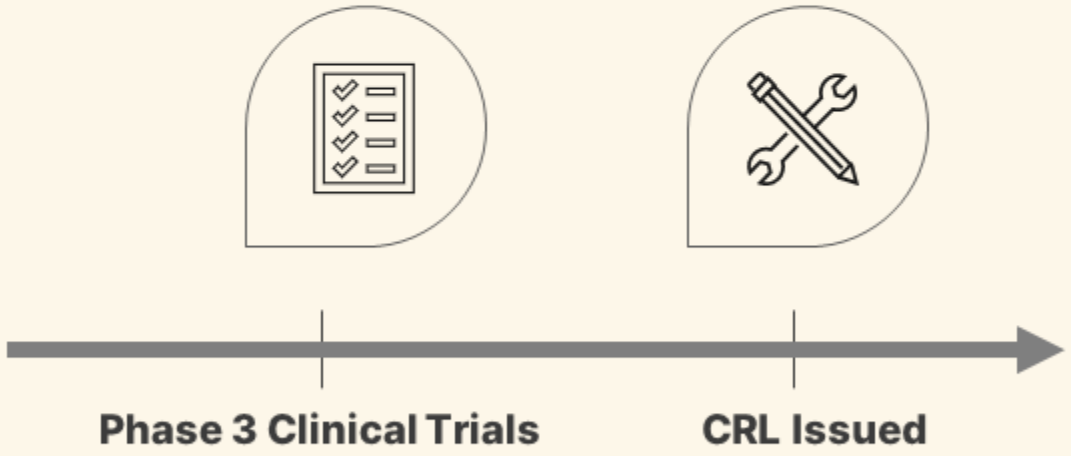
Source: Bloomberg, Clinical Trial Gov.

Best-in-Class Clinical Data

- ✓ As of now, Rivoceranib/Camrelizumab has the highest overall survival (OS) period among HCC 1st line market, with **23.8 months.**
- ✓ Rivoceranib/Camrelizumab demonstrates high efficacy across all patient groups, regardless of the HCC incidence risk factors.
- ✓ In the first-line liver cancer treatment market, Atezolizumab/Bevacizumab, with the highest market share for now, exhibits efficacy primarily in patients with ALBI grade 1. In contrast, Rivoceranib/Camrelizumab demonstrates efficacy in patients with all ALBI grades 1 and 2, with notably superior effectiveness, particularly in ALBI grade 2 patients where Atezolizumab/Bevacizumab shows less to no efficacy.
- ✓ Rivoceranib/Camrelizumab has the lowest clinical discontinuation rate in HCC 1st market. The likelihood of treatment discontinuation due to side effects is very low.
- ✓ With a very short drug half-life of about 11 hours compared to other competitors, is easy to discontinue and manage side effects, and has a significantly lower risk of side effects.

Expandability of Indications

The Status of Phase 3 Clinical Trials (Rivoceranib)



Market Size of Indications

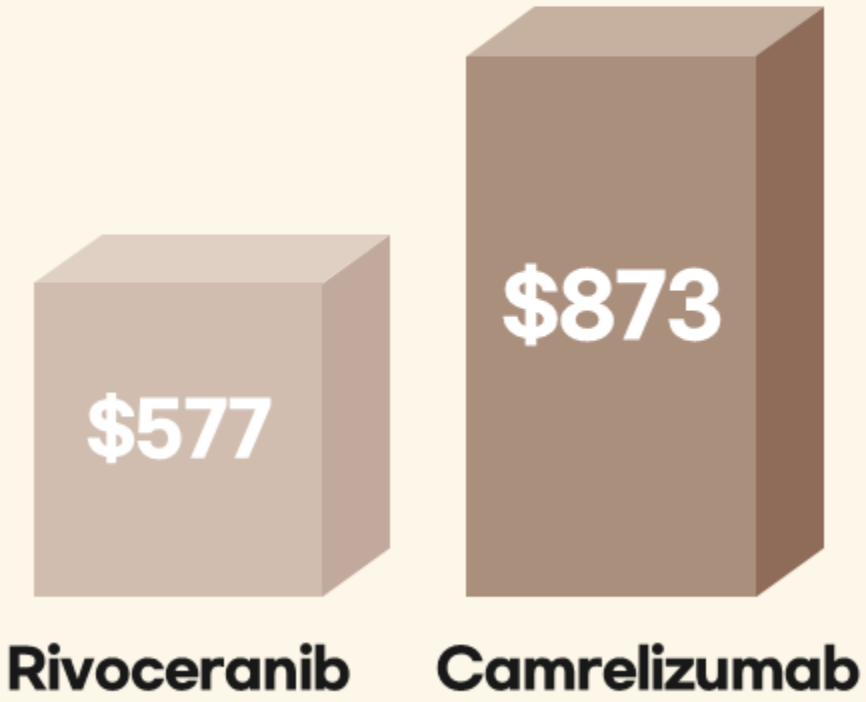
Indication	Market Size (2022)
Adjuvant/Neoadjuvant For HCC	$5 Billions
TACE	$10 Billions
GC 1ST Line	$6 Billions
Ovarian Cancer 2nd Line	$7 Billions
Breast Cancer 2nd Line	$28 Billions
Prostate Cancer 1st Line	$13 Billions

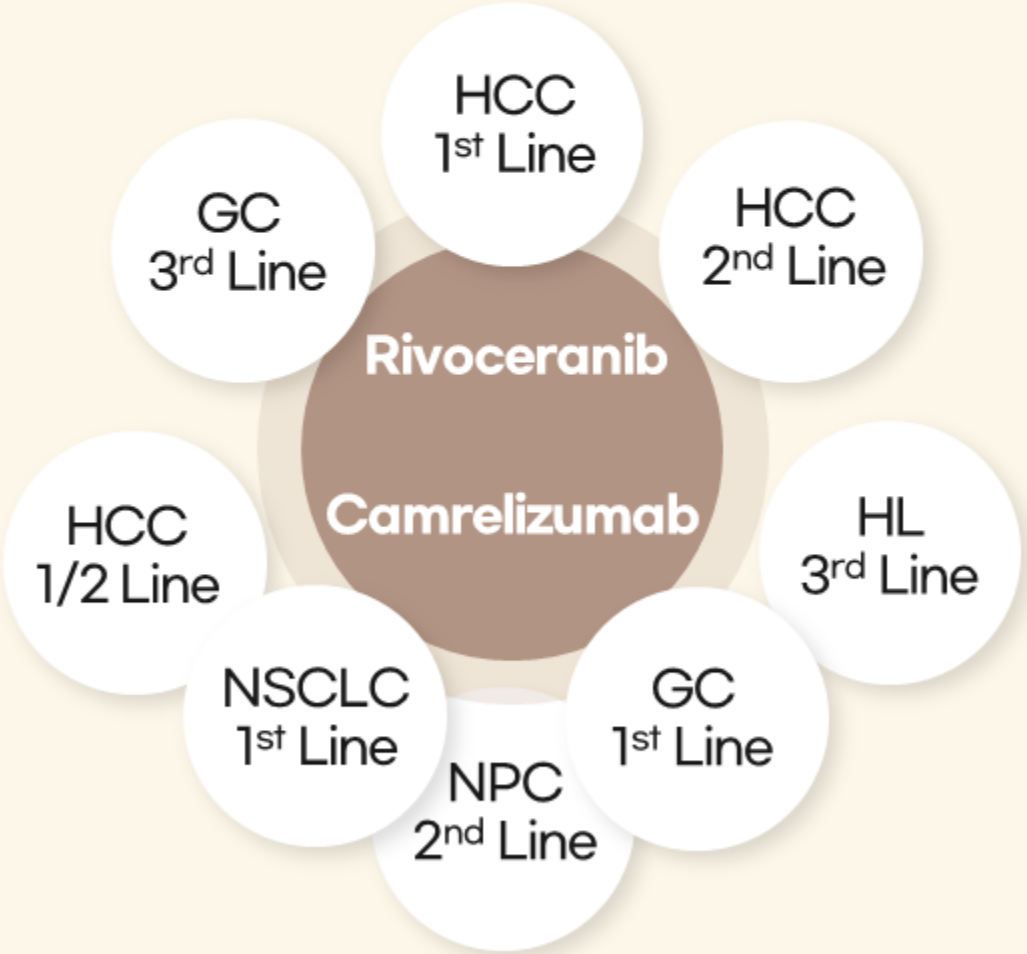
HCC=Hepatocellular Carcinoma, TACE= Transarterial Chemoembolization

Expandability of Indications

Revenue in China (2023)

Unit: USD Million





HCC=Hepatocellular Carcinoma, GC= Gastric Cancer, NSCLC= Non Small Cell Lung Cancer, NPC= Nasopharyngeal Carcinoma, HL= Hodgkin's Lymphoma

We Are Ready To Go: Targeting 7 Regions and 59 Subregions

Concept: "Enhanced Quality of Life through Extended Survival"

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