

BRINGING FRUQUINTINIB TO MORE PATIENTS GLOBALLY

January 2023

Nasdaq/AIM: HCM; HKEX: 13



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Dr Weiguo Su

Chief Executive Officer and Chief Scientific Officer
HUTCHMED

HUTCHMED's deep & broad portfolio

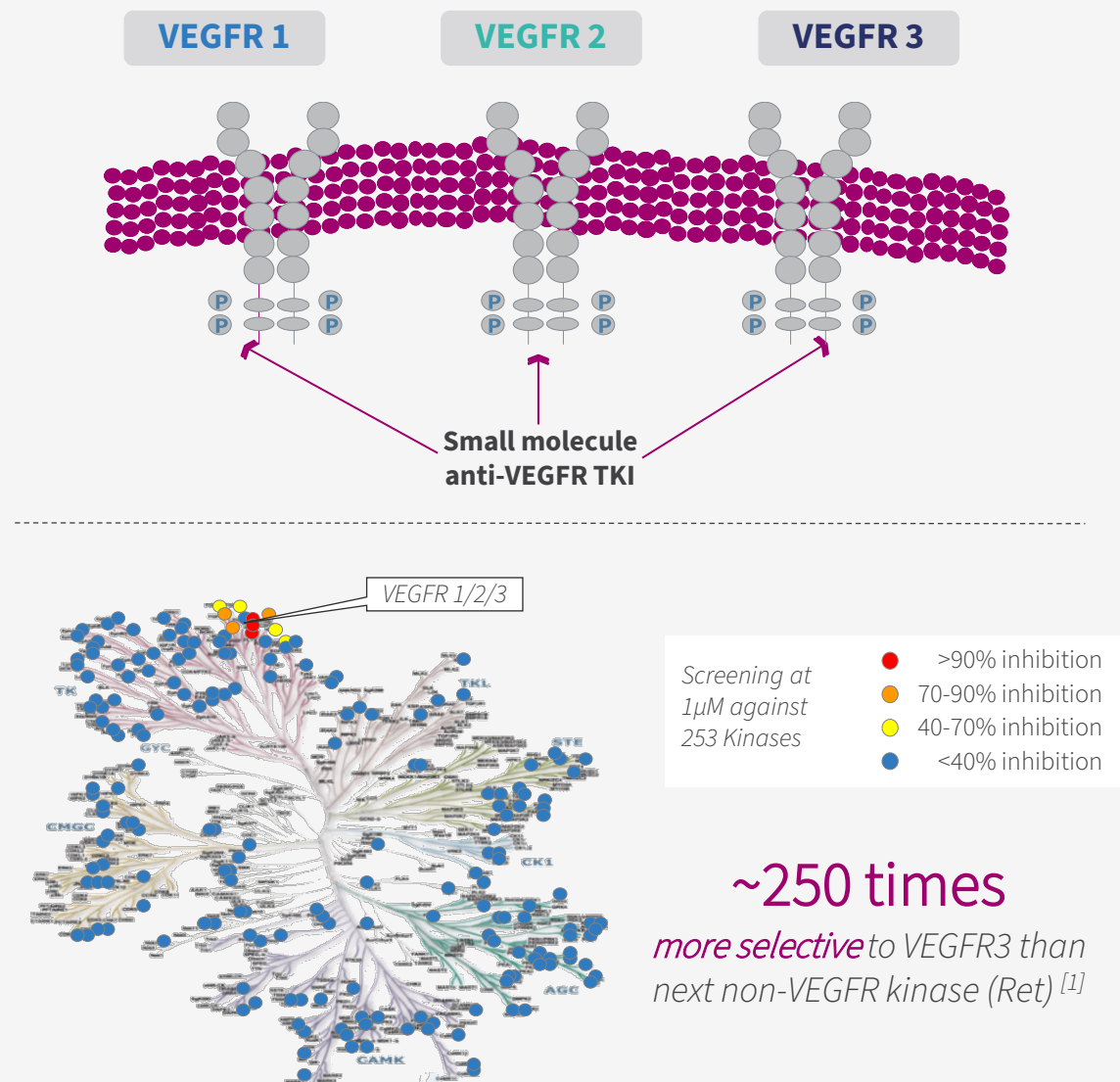
Mostly discovered in-house

PRODUCT	MOA	INDICATIONS	PARTNER	CHINA ^[1]	GLOBAL ^[1]
Fruquintinib	VEGFR 1/2/3	Colorectal, gastric, EMC, RCC (multiple I/O & TKI combos)	 (China) ^[3]  (Ex-China) ^[4]	Marketed (Colorectal); Pending NMPA discussion (Gastric) Ph.III ongoing (RCC) Ph.II reg-intent ongoing (EMC)	Preparing filings in U.S., E.U., Japan based on positive MRCT (Colorectal)
Surufatinib	VEGFR 1/2/3, FGFR1 & CSF-1R	NET, NEC (multiple I/O combos)	None ^[6]	Marketed (NET, pNET) Ph.III (NEC)	Ph. III ready US, EU PMDA consultation for JNDA filing
Savolitinib	MET	NSCLC, kidney, gastric, colorectal ^[2] (multiple I/O & TKI combos)	 (Worldwide) ^[5]	Marketed (NSCLC mono) Ph.III (NSCLC combo) Ph.II reg-intent (Gastric)	Ph.II/III global (multiple NSCLC) Ph.III global (PRCC)
Amdizalisib	PI3Kδ	B-cell malignancies – indolent NHL	None ^[6]	Ph.II reg-intent (FL & MZL)	Ph. II
Sovleplenib	Syk	ITP, B-cell malignancies	None ^[6]	Ph. III (ITP) TBD (NHL)	Ph. II
Tazemetostat	EZH2	Solid tumors, hematological malignancies	 (ex-China) ^[7]	Marketed (ES & FL, Hainan) Bridging (3L FL) Global Ph. Ib/III (2L FL combo)	Marketed by Ipsen ^[8]
HMPL-453	FGFR 1/2/3	Cholangiocarcinoma	None	Ph.II reg-intent study in preparation	-
HMPL-306	IDH 1/2	Hematological malignancies, solid tumors	None ^[6]	Ph. I	Ph. I
HMPL-295	ERK (MAPK pathway)	Solid tumors	None	Ph. I	-
HMPL-760	3G BTK	Hematological malignancies	None ^[6]	Ph. I	Ph. I
HMPL-653	CSF-1R	Solid tumors	None	Ph. I	-
HMPL-A83	CD47	mAb – solid tumors, hematological malignancies	None	Ph. I	-

[1] Represents the most advanced clinical trial stage and indication; [2] Investigator initiated trials (IITs); [3] HCM has WW rights ex-China; Subject to meeting pre-agreed sales targets, Lilly will pay HUTCHMED an estimated total of 70%-80% of ELUNATE® sales in the form of royalties, manufacturing costs and service payments; [4] subject to customary closing conditions, including completion of antitrust reviews; [5] AZ has WW rights: China (30% royalty), ex-China (9-18% tiered royalty); [6] Open to partnering outside of Greater China ; [7] HCM has commercial & development rights in Greater China; [8] Tazemetostat was developed by and is marketed in the U.S. by Epizyme, Inc., which was acquired by Ipsen SA in August 2022.

Fruquintinib is highly selective to VEGFR

Efficacy with limited off-target toxicity



- **Potent against VEGFR1,2,3**, resulting in consistent clinical benefit for patients who failed bevacizumab
- **Highly selective** vs. other kinases with good safety profile with readily manageable AEs
- **Combination studies** with chemo, targeted therapies and IO

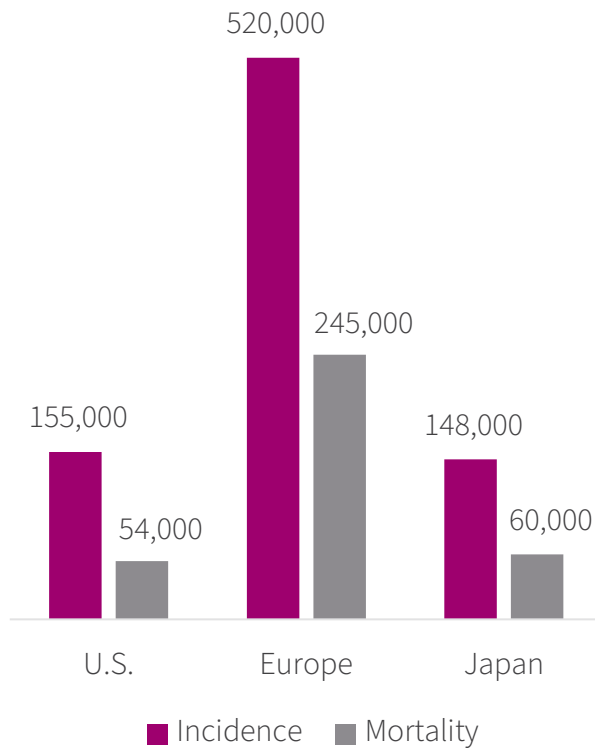
3rd-Line Metastatic Colorectal Cancer	FRESCO Phase III (China)	
Treatment arms	ELUNATE®	Placebo
≥G3 AE (Safety population)	61.1%	19.7%
VEGFR on-target related AEs ≥ G3:		
Hypertension	21.2%	2.2%
Hand-Foot Syndrome	10.8%	0.0%
Off-target (i.e. non-VEGFR) related AEs ≥ G3:		
Hypophosphatemia	0.0%	1.5%
Hypokalemia	0.7%	0.7%
Rash/desquamation	0.0%	0.0%
Lipase increase	0.0%	0.0%
Hepatic function (Liver function) AEs ≥ G3:		
ALT increased	0.7%	1.5%
AST increased	0.4%	0.7%
Blood bilirubin increased	1.4%	1.5%

[1] Sun et al., Cancer Biology & Therapy 15:12, 1635--1645; December 2014.

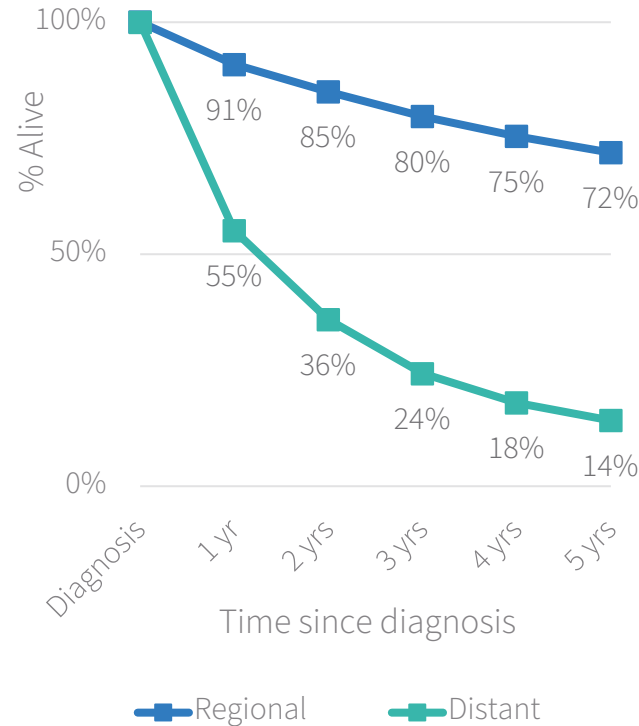
Colorectal cancer a significant burden...

...but there are still limited treatment options for most patients

High CRC incidence and deaths across the globe ^[1]



Patients with advanced CRC have lower relative survival rate ^[2]



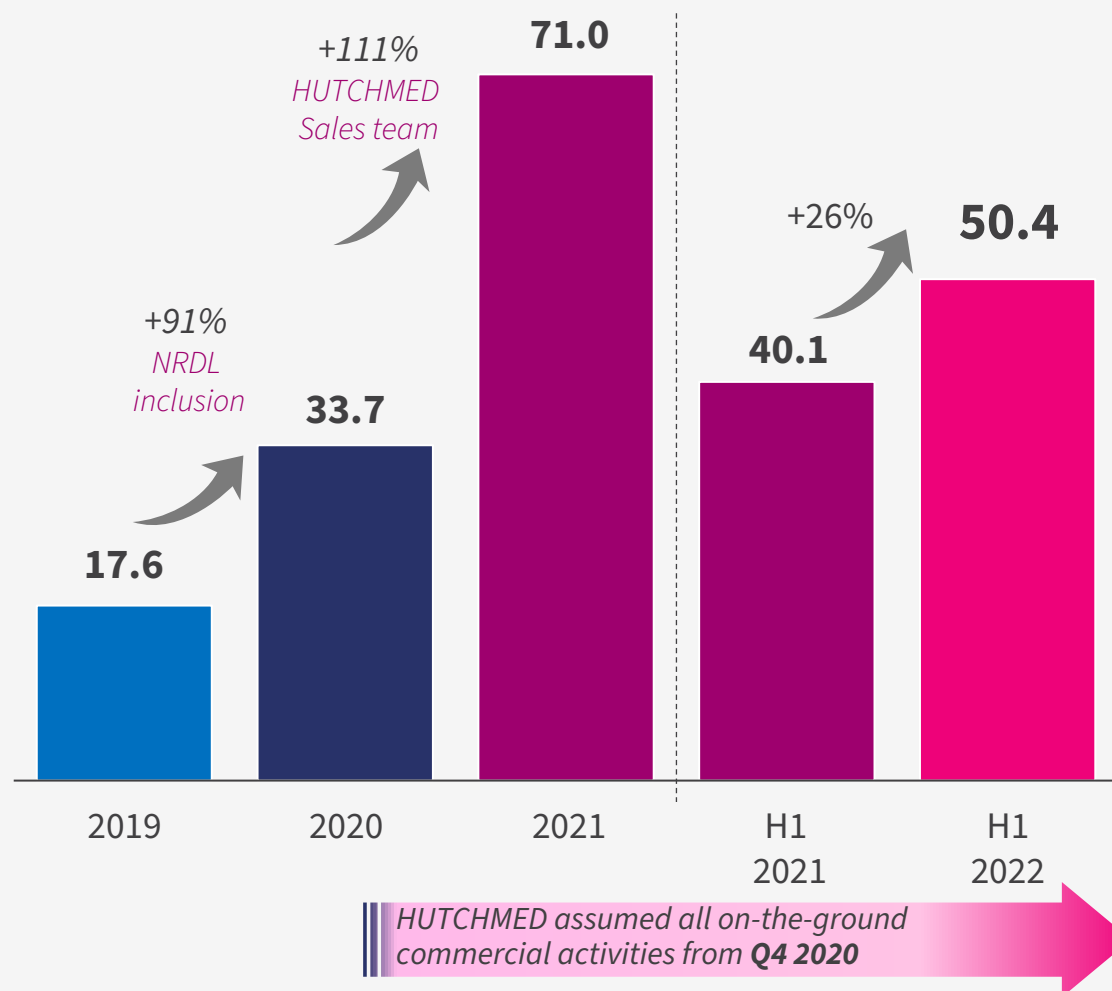
Unmet medical need

- **Limited use of approved 3L treatments**
 - Regorafenib (approved Q3 2012)
 - TAS-102 (approved Q3 2015)
- **Chemotherapy, anti-VEGF & anti-EGFR agents used across all lines**
- **Newer treatment options focus on discrete actionable mutations**
 - ~10% of patients have BRAF mutation ^[3]
 - ~15% of patients have MSI-H or dMMR disease ^[4]

Fruquintinib is the market leader in 3L CRC in China

Over 50,000 patients treated to date

In-market sales (US\$ millions)



Continued progress in H1 2022

- ~14,000 est. new patients treated, up ~40% versus H1 2021
- >RMB1bn in cumulative in-market sales since launch 3½ years ago

Strong competitive position

- 2022 NRDL renewal
- Patient share market leader in 3L CRC (IQVIA^[1]) despite later launch

	Q4-18	Q4-19	Q4-20	Q4-21	Q4-22
ELUNATE®	2%	25%	33%	39%	44%
STIVARGA®	29%	32%	35%	34%	29%

[1] IQVIA audit data in proprietary post-launch research panel of mainly Class 3 hospitals in Top 30 cities in China

Vision: bringing fruquintinib to patients globally

While advancing other opportunities

- Bandwidth and extended cash runway to advance other opportunities

- Completed multi-regional clinical trial
- Initiated rolling NDA submission to FDA in Dec 2022

- Partner with  for fruquintinib development and commercialization ex-China



- Designed & synthesized fruquintinib
- Completed RCT leading to registration in China

- Commercializing fruquintinib in China
- Achieved 43% market share within 4 years of launch
- Multiple active LCM programs



Fruquintinib global MRCT, FRESCO-2 – positive data at ESMO

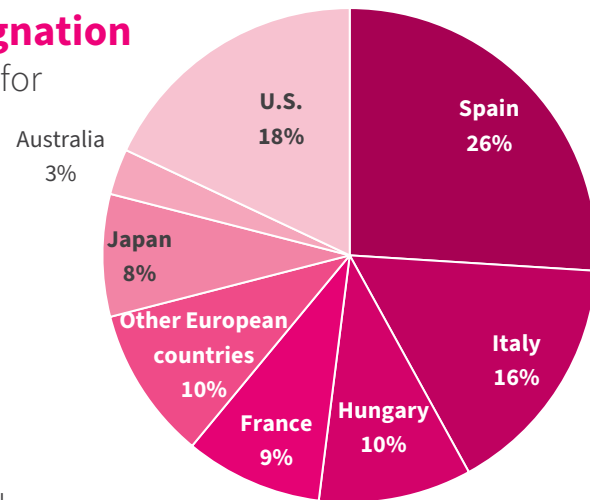
FRESCO-2 MRCT started after regulatory consultation in U.S., Europe & Japan

• U.S. Fast Track Designation

for $\geq 3L$ mCRC & potential for rolling submission

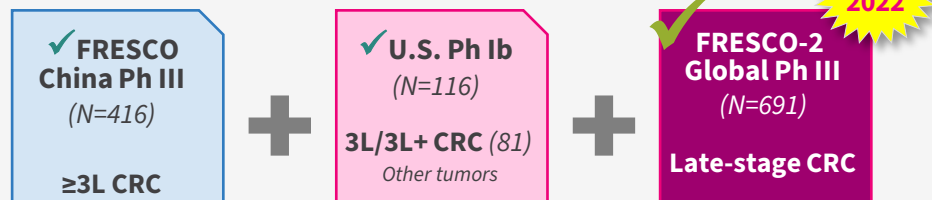
• Primary endpoint is overall survival

- 691 patients
- ~150 sites
- 14 countries
- Recruited in ~15 months



Fruquintinib – Basis for global filings

Aggregation of China, U.S. & global studies



Consistency of effect across late-stage settings enriches the continuum of care

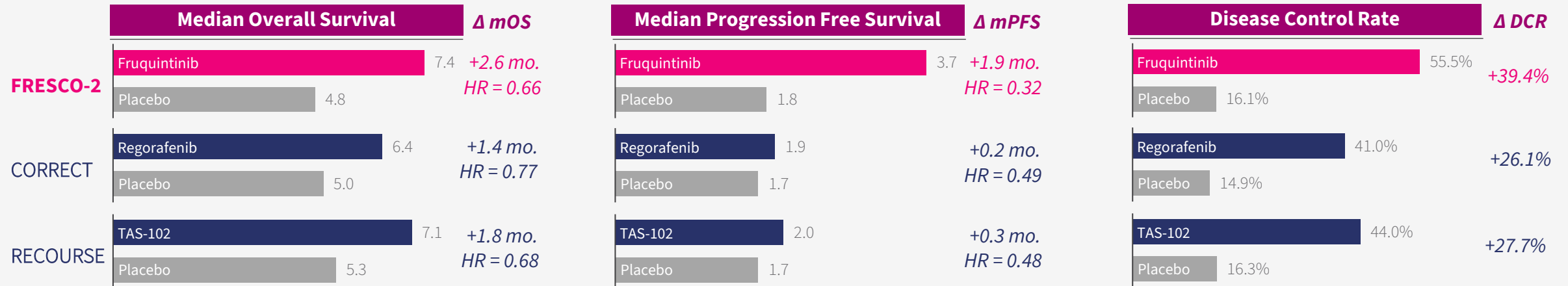
	FRESCO-2 [1]		FRESCO [2]	
	Fruq (n=461)	Placebo (n=230)	Fruq (n=278)	Placebo (n=138)
Prior Tx				
VEGFi	97%	96%	30%	30%
EGFRi as % of RASwt	>100%	>100%	~25%	~25%
TAS-102	52%	53%	0%	0%
Regorafenib	9%	8%	0%	0%
Both TAS-102 & rego	39%	40%	0%	0%
mOS, mo.	7.4	4.8	9.3	6.6
[95% CI]	[6.7-8.2]	[4.0-5.8]	[8.2-10.5]	[5.9-8.1]
HR	0.66		0.65	
(95% CI, p-value)	(0.55-0.80, p<0.001)		(0.51-0.83, p<0.001)	
mPFS, mo.	3.7	1.8	3.7	1.8
[95% CI]	[3.5-3.8]	[1.8-1.9]	[3.7-4.6]	[1.8-1.8]
HR	0.32		0.26	
(95% CI, p-value)	(0.27-0.39, p<0.001)		(0.21-0.34, p<0.001)	
DCR	55.5%	16.1%	62.2%	12.3%

DCO: June 24, 2022

DCO: January 17, 2017

Fruquintinib has a highly competitive profile

FRESCO-2 results have potential to change clinical practice worldwide



Fruquintinib is well tolerated with a safety profile consistent with the previously established monotherapy profile

Tolerability	FRESCO-2 ^[1]		CORRECT ^[2]		RECOURSE ^[3]	
	Fruquintinib	Placebo	Regorafenib	Placebo	TAS-102	Placebo
Discontinuation due to AE	20%	21%	17%	12%	4%	2%
TEAE Grade \geq 3	63%	50%	54%	14%	69%	52%
Major TEAE Grade \geq 3						
Hypertension	14%	1%	7%	1%	n/a	n/a
Hand-foot syndrome	6%	0%	17%	<1%	n/a	n/a
Asthenia / fatigue	8%	4%	15%	9%	7%	9%
Other AEs of note	n/a		<ul style="list-style-type: none"> Blackbox warning on hepatotoxicity Monitor liver function prior to and during treatment 		<ul style="list-style-type: none"> Severe myelosuppression Obtain complete blood counts prior to and on day 15 of each cycle 	

Note: Illustrative comparison only. No head-to-head studies have been conducted. Study parameters differ.

[1] ESMO 2022, LBA25; [2] Grothey A, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet*. 2013;381(9863):303-312. doi:10.1016/S0140-6736(12)61900-X; [3] Mayer RJ, et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. *N Engl J Med*. 2015;372(20):1909-1919. doi:10.1056/NEJMoa1414325.

Bringing Fruquintinib to more patients globally

Fruquintinib license financial terms

Upfront	<ul style="list-style-type: none">• US\$400 million
Development, Regulatory & Sales Milestones	<ul style="list-style-type: none">• Up to \$730 million
Royalties	<ul style="list-style-type: none">• Based on annual net sales• Tiered royalties• Consistent with commercial-launch stage licensing transactions

Strategic collaboration accelerates HUTCHMED's strategy

- Validates our high confidence in the future success and commercial opportunity of fruquintinib, while allowing us to share in that success
- Accelerates and broadens development and potential commercialization of fruquintinib
- Adds resources to advance our deep oncology pipeline

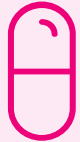
Robust development plans with clear path to commercialization

Fruquintinib license summary

Included in collaboration	<ul style="list-style-type: none"> Development, manufacturing, selling & marketing 	
Territories	<ul style="list-style-type: none"> U.S., Japan, Europe & RoW except China HUTCHMED continues to develop & market fruquintinib in China 	
Regulatory Filings	<ul style="list-style-type: none"> Complete U.S. NDA rolling submission in H1 2023 Submit MAA in Europe in 2023 Submit JNDA to the Japan PMDA in 2023 	
Commercial Launch	<ul style="list-style-type: none"> Collaboration accelerates development and global commercialization Takeda initiating launch readiness 	
Further Clinical Development (LCM)	<ul style="list-style-type: none"> Indications beyond mCRC being evaluated HUTCHMED ongoing programs in China may inform decisions 	

Takeda is the right partner for HUTCHMED to maximize the potential of fruquintinib


HUTCHMED



Clinical development & regulatory operations in all major markets



Global novel drug discovery & manufacturing operations



Commercial capabilities in China



Industry leader with global oncology and GI presence



Consistent track record of success



Shared values and ambitions

Takeda: A Global Biopharmaceutical Company



HEADQUARTERS
TOKYO, JAPAN

GLOBAL HUB
**CAMBRIDGE,
MA, USA**

~40 NEW MOLECULAR
ENTITY CLINICAL
STAGE ASSETS

PRESENCE: APPROX. IN
80 COUNTRIES
& REGIONS

30+ MANUFACTURING
SITES

3 RESEARCH
SITES

200+
PARTNERSHIPS TO HELP
US BRING INNOVATION
TO PATIENTS

TOP EMPLOYER® IN

39

COUNTRIES & 4 REGIONS

FY21 REVENUE



Convenience translation of reported JPY figures into USD using rate of 121.44 JPY/USD, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 31, 2022.

FOUNDED IN

1781

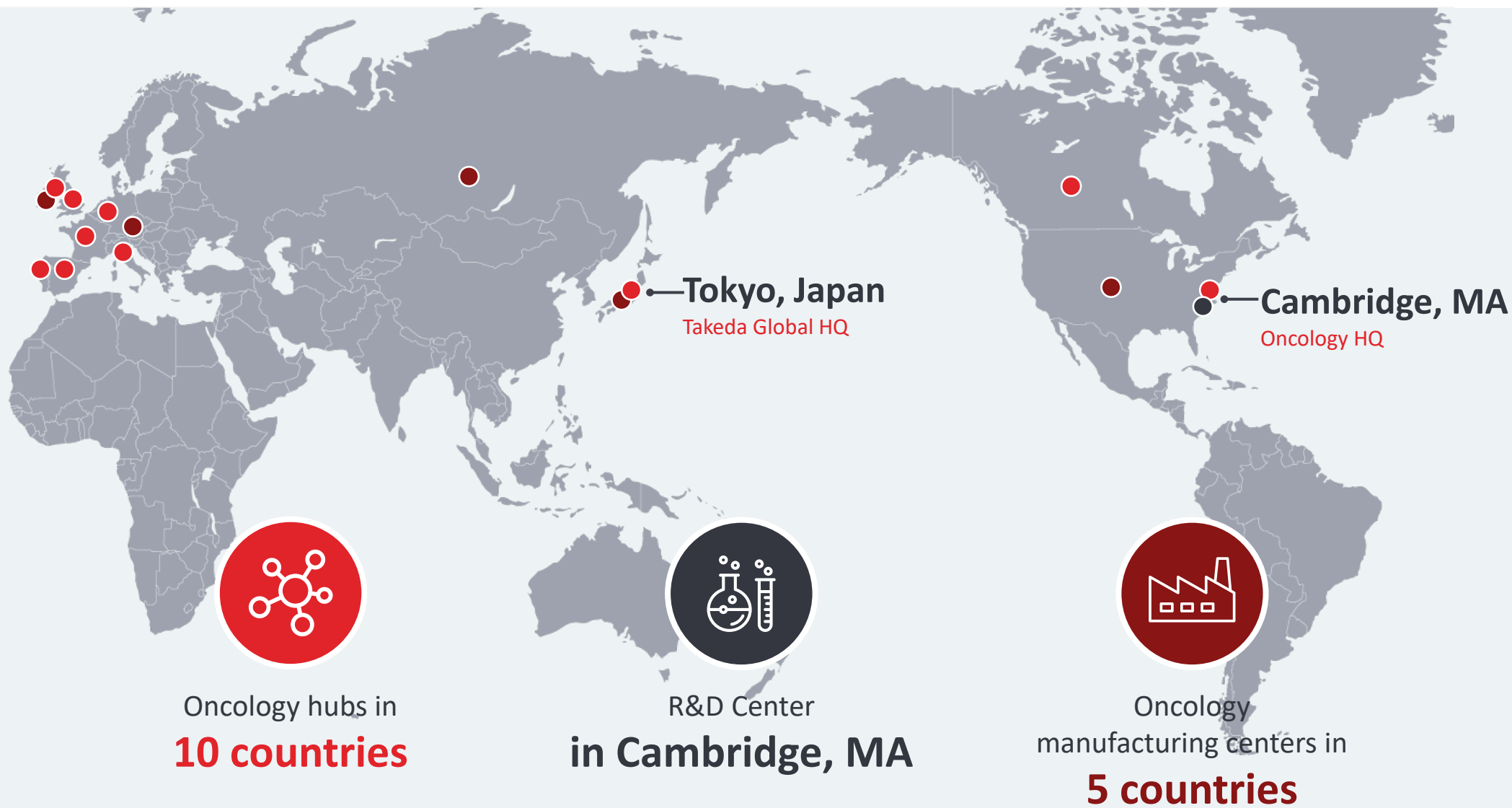
OSAKA, JAPAN

PEOPLE



UNLESS OTHERWISE NOTED ALL NUMBERS AS OF JUNE 2022

Takeda's Oncology Business Unit has a strong global presence



Deep legacy in hematologic cancers; growing portfolio in solid tumors

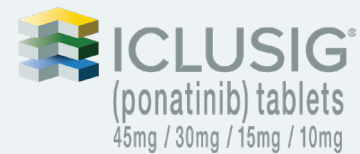


Best-in-class development and commercialization capabilities in oncology

Global



U.S.








Japan



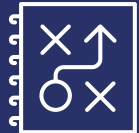
Europe



Fruquintinib registration/potential registration studies

STUDY	TARGET DISEASE / DESIGN (N, ARMS, 1° ENDPOINT)	REGION	STATUS	EST. (S)NDA FILING IF POSITIVE
FRESCO-2	Adv colorectal cancer 691, treatment vs. BSC, OS	Global 	US, EU, Japan submissions completion planned for 2023	Started Dec 22
FRESCO	3L+ colorectal cancer 416, treatment vs. BSC, OS	China 	Launched in China in 2018	2017
FRUTIGA	2L GC, combo with chemo 703, combo vs. chemo, OS & PFS	China 	To file sNDA in China	H1 2023
2L EMC	2L EMC, combo with PD-1 / ~130, 1 arm, ORR	China 	FPI Oct 21	2024
2L RCC	2L RCC, combo with PD-1 / ~260, 2 arms, PFS	China 	FPI Oct 22	2025

- **Global vision unchanged:** bringing our innovative medicines to patients worldwide
- **10+ NDA** submissions in plan, in China & globally
- Continue our **strong China commercial** momentum



Strategic focus

- **Remain agile**
- **Prioritize** late-stage programs, registration studies & regulatory approvals
- **Commercial partnering internationally** to expedite access to our medicines globally



Build on our strengths

Bring near-term value

Build a long-term sustainable business

- Rapidly growing China sales
- Deliver the next wave of new product registrations
 - Fruquintinib globally ex-China
 - Sovleplenib, amdizalisib & tazemetostat in China
- **Path to profitability**

Q & A Session

HUTCHMED management



Dr Weiguo Su

Chief Executive Officer and Chief Scientific Officer
HUTCHMED



Mr Johnny Cheng

Chief Financial Officer
HUTCHMED



Dr Karen Atkin

Chief Operating Officer
HUTCHMED



Dr Michael Shi

Head of R&D and Chief Medical Officer
HUTCHMED

Takeda representative



Pallavi Garg

Head of Global Oncology Products and Pipeline Strategy
Takeda

Thank you



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