# COMMERCIAL, REGULATORY & CLINICAL PROGRESS UPDATE

#### H1 2021 RESULTS

July 28, 2021

Nasdaq/AIM:HCM | HKEX:13





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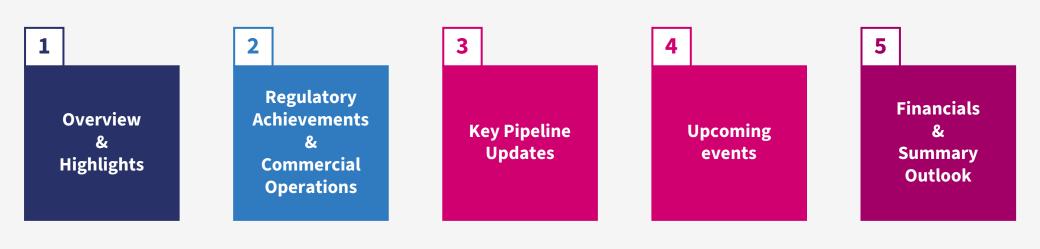
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Use of Non-GAAP Financial Measures - This presentation includes certain non-GAAP financial measures. Please see the appendix slides titled "Non-GAAP Financial Measures and Reconciliation" for further information relevant to the interpretation of these financial measures and reconciliations of these financial measures to the most comparable GAAP measures.

# Agenda



# Review of H1 progress and 2021-22 outlook





# **1. OVERVIEW OF H1 HIGHLIGHTS**

# Building a global science-focused biopharma



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Global novel oncology **drug discovery & manufacturing** operations based **in China** 

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Clinical development and regulatory operations in all major markets

In-house **commercial in China & U.S.** – self-determination in about half of global pharma market



Commercial partnerships in rest of the world markets



# **Differentiated portfolio**



# All discovered in-house & designed for global differentiation

PRODUCT	MOA	DISCOVERY <sup>[1]</sup>	INDICATIONS	PARTNER	RIGHTS	CHINA <sup>[2]</sup>	GLOBAL <sup>[2]</sup>
Surufatinib (SULANDA®)	VEGFR 1/2/3, FGFR1 & CSF-1R	In-house (est. LOE ~2035)	Neuroendocrine tumors (NET), biliary tract, thyroid, solid tumors (multiple I/O combos)	None	HCM holds all WW rights	Marketed (non-pNET) Marketed (pNET)	U.S. NDA accepted E.U. MAA accepted
Fruquintinib (ELUNATE®)	VEGFR 1/2/3	In-house (est. LOE ~2033)	Colorectal, gastric, NSCLC, solid tumors (multiple I/O & TKI combos)	Lilly	HCM has WW rights ex- China; 70%-80% of sales in China <sup>[4]</sup>	Marketed (Colorectal); Ph.III (Gastric)	Ph.III U.S., E.U., Japan (Colorectal)
Savolitinib (ORPATHYS®)	MET	In-house (est. LOE ~2035)	NSCLC, kidney, gastric <sup>[3]</sup> , colorectal <sup>[3]</sup> (multiple I/O & TKI combos)	<b>§</b>	AZ has WW rights; China (30% royalty); ex-China (9- 18% tiered royalty)	Marketed (NSCLC mono) Ph.III (GC, NSCLC combo*)	Ph.II/III global (multiple NSCLC) Ph.III global (PRCC*)
HMPL-689	ΡΙ3Κδ	In-house (est. LOE ~2040)	B-cell malignancies – indolent NHL	None	HCM holds all WW rights	$\textbf{Ph.II reg-intent} \; (\textsf{FL} \And \textsf{MZL})$	<b>Ph.I</b> U.S., E.U., Aus (NHL)
HMPL-523	Syk	In-house (est. LOE ~2037)	ITP, B-cell malignancies – indolent non-Hodgkin's lymphoma (NHL)	None	HCM holds all WW rights	<b>Ph.Ib/II</b> (Treated >200 NHL pts.)	Ph.I U.S., E.U., Aus (NHL)
HMPL-453	FGFR 1/2/3	In-house (est. LOE ~2039)	Cholangiocarcinoma	None	HCM holds all WW rights	Ph.II (IHCC)	-
Epitinib	EGFRm+	In-house (est. LOE ~2032)	Glioblastoma	None	HCM holds all WW rights	Ph.II (Glioblastoma)	-
HMPL-306	IDH 1/2	In-house (est. LOE ~2043)	Hematological malignancies, solid tumors	None	HCM holds all WW rights	Ph.I (Hem. malignancies)	<b>Ph.I</b> (solid tumor & hem. malignances)
HMPL-295	ERK (MAPK pathway)	In-house	Solid tumors	None	HCM holds all WW rights	Ph.I (Solid tumors)	-
HMPL-760	3G BTK	In-house	Hematological malignancies	None	HCM holds all WW rights	IND submitted June 2021	IND submitted June 2021
HMPL-653	CSF-1R	In-house	Solid tumors	None	HCM holds all WW rights	Target IND 2023	(U.S./China)
HMPL-A83	CD47	In-house	mAb – solid tumors, hematological malignancies	None	HCM holds all WW rights	Target IND 2021	. (U.S./China)

\*In planning

[1] Approximate estimated Loss of Exclusivity (LOE) in key markets considering multiple patent families, extension, and regulatory protection; [2] Represents the most advanced clinical trial stage and indication; [3] Investigator initiated trials (IITs); [4] Subject to meeting pre-agreed sales targets, Lilly will pay HUTCHMED an estimated total of 70%-80% of ELUNATE<sup>®</sup> sales in the form of royalties, manufacturing costs and service payments.

# H1 highlights



#### Regulatory & Commercial

- H1 2021 revenues: Oncology/Immunology up 161% to \$42.9m
- ORPATHYS<sup>®</sup> (savolitinib):
   1<sup>st</sup> approval & launch in July
- ELUNATE<sup>®</sup> (fruquintinib): In-market sales up +186%\*
- SULANDA<sup>®</sup> (surufatinib): Launches now for NETs of any primary tumor origins
- Surufatinib ex-China: U.S. NDA & E.U. MAA accepted

#### Pipeline

- Savolitinib: Starting 5 new global & China registration studies in 2021
- Surufatinib & Fruquintinib: PD-1 combos entering registration studies
- Transitioning Pipeline in Hematology: HMPL-689 (PI3Kδ) now in late stage
- Early-stage Pipeline & Discovery Research: 5 new inhouse clinical assets 2020-2021 (IDH1/2, ERK, CD47, 3G BTK, & CSF-1R)

#### Organizational Progress

• International R&D Organization and U.S. Commercial:

Continuing to build for potential surufatinib launch H1 2022 and growing pipeline

- China Commercial: Scaling rapidly to ~600 staff by YE
- Building New Flagship Manufacturing Facility: Designed for >5X increase small molecule capacity & mAb capability starting 2024
- ~\$1.2bn cash & resources



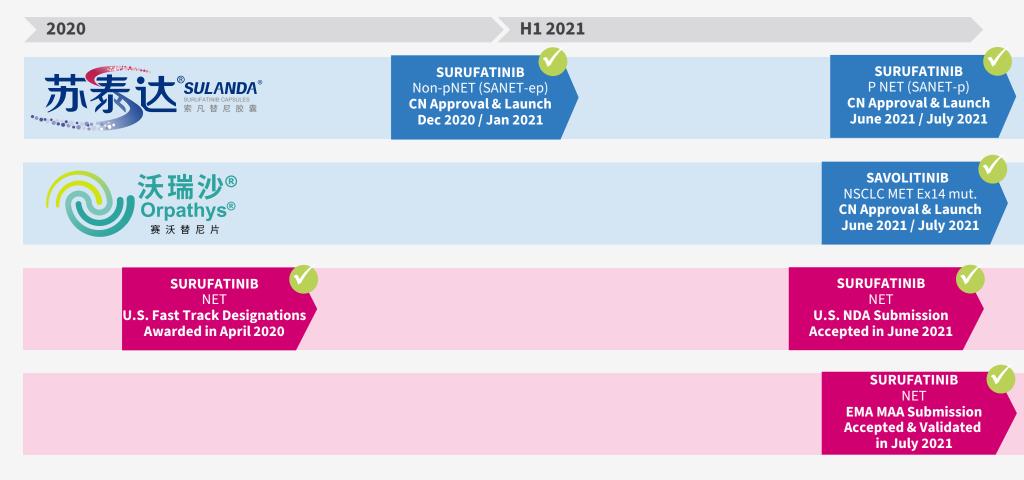
# 2. ONCOLOGY REGULATORY ACHIEVEMENTS & COMMERCIAL OPERATIONS

ELUNATE<sup>®</sup> *(fruquintinib brand in China)* SULANDA<sup>®</sup> *(surufatinib brand in China)* ORPATHYS<sup>®</sup> *(savolitinib global brand)* 

# Major regulatory achievements



# Progress in China, U.S., and Europe





# **China Commercial operations infrastructure**

# Leverages scale and capabilities from multiple affiliates

# HUTCHMED

#### Oncology team

- ✓ 540+ (and growing) sales reps
- ✓ 2,500+ oncology hosp./clinics
- ✓ 29,000+ oncology physicians

#### Shanghai Hutchison Pharmaceuticals

Nationwide distribution & promotion

- ✓ 2,200+ sales reps
- ✓ 23,000+ hospitals
- ✓ 83,000+ physicians

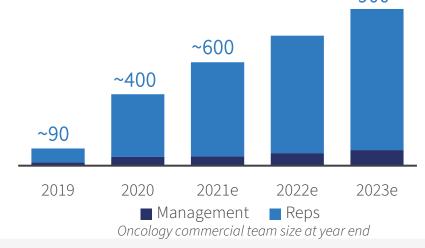
#### Hutchison Sinopharm Pharmaceuticals

- Third-party distribution & logistics
- Nationwide support from Sinopharm in distribution/logistics
- Deep Shanghai coverage

#### Expanding rapidly to support ELUNATE<sup>®</sup> & SULANDA<sup>®</sup> launches

#### 2,500+ oncology hospitals and 29,000+ oncology physicians covered

- Fully in-place since mid-2020;
- Vast majority of new staff from successful China oncology companies (MNC & locals)
- Expansion planned for future product launches
- SF productivity targeted to reach to US\$400k per Rep. per year in 2023
   900+

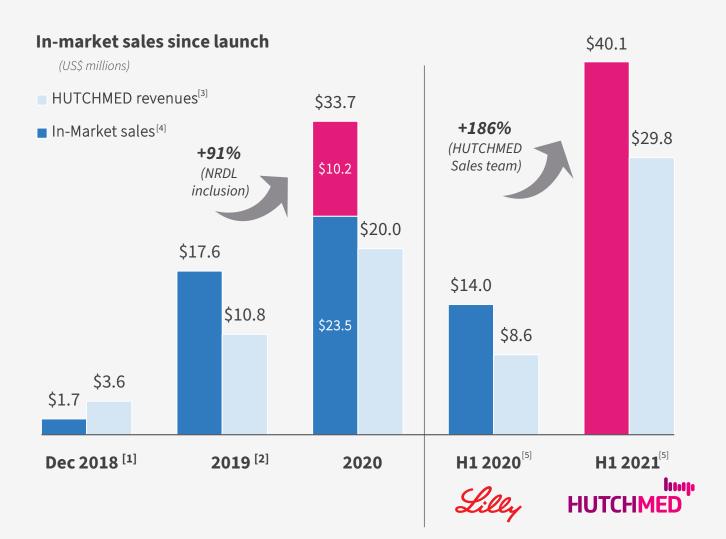


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# **ELUNATE® commercial update**

# HUTCHMED oncology sales team have made instant impact





HUTCHMED Sales team assumed all on-the-ground execution responsibilities in Q4 2020

Fruquintinib Capsules

**~5,000** educational / scientific events in H1 2021

~83,000 new patients/yr. estimated China incidence of 3L CRC

Est. ~9,000 patients treated in H1 2021

[1] ELUNATE® was launched in late November 2018. HUTCHMED revenues in 2018 primarily relate to manufacturing fees and royalties paid by Lilly.

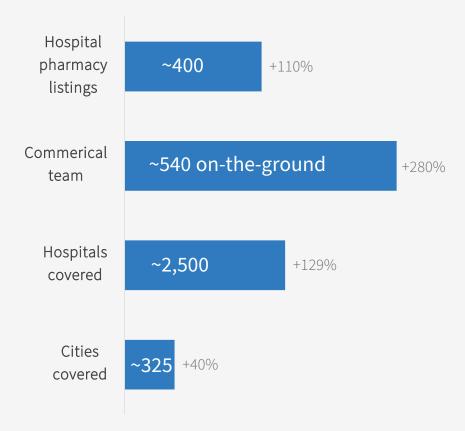
[2] During Q4 2019, ELUNATE® in-market sales were affected by rebates and downward price adjustments required in the distribution channel in the lead up to NRDL inclusion effective Jan 1, 2020;

[3] Represents manufacturing fees, commercial service fees and royalties paid by Lilly to HUTCHMED and sales to other third parties invoiced by HUTCHMED; [4] Represents total sales to third parties as provided by Lilly; [5] Unaudited.

# **ELUNATE® coverage and key opportunities**

Sales benefitting from deeper coverage...

# Increased on-the-ground activities June 30, 2021 vs. Sept 30, 2020



# ... of approved indications

• CRC: 2<sup>nd</sup> highest cancer incidence in China, with up to 550,000 new patients in 2020<sup>1</sup>

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Fruquintinib Capsules

• 3L CRC patients increasing quickly

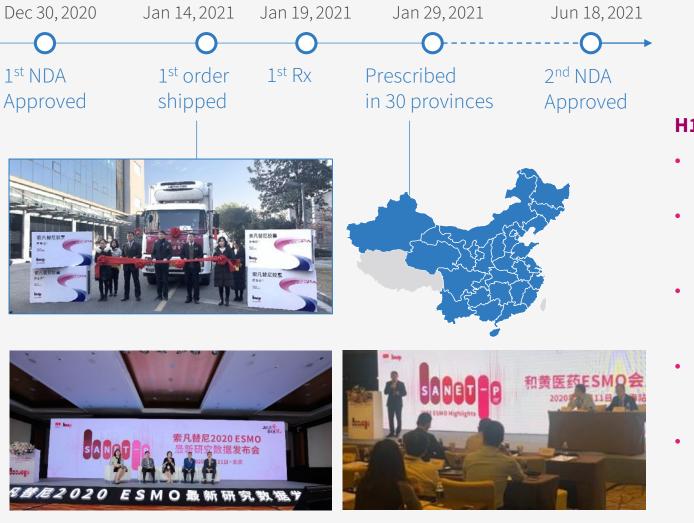
# Clinical development programs in multiple new indications

- **Promising ELUNATE® PD-1 combo data** presented at ASCO 2021, may lead to initiation of additional registration studies
- ~20 investigator-initiated trials (IITs) ongoing exploring treatment of 2L CRC patients intolerant to chemotherapy
- Phase III in 2L gastric cancer (GC) ongoing

# SULANDA® initial progress encouraging



# 2 NDAs approved in 6 months, leading to \$8.0m<sup>[1]</sup> in 1<sup>st</sup> half-year on market



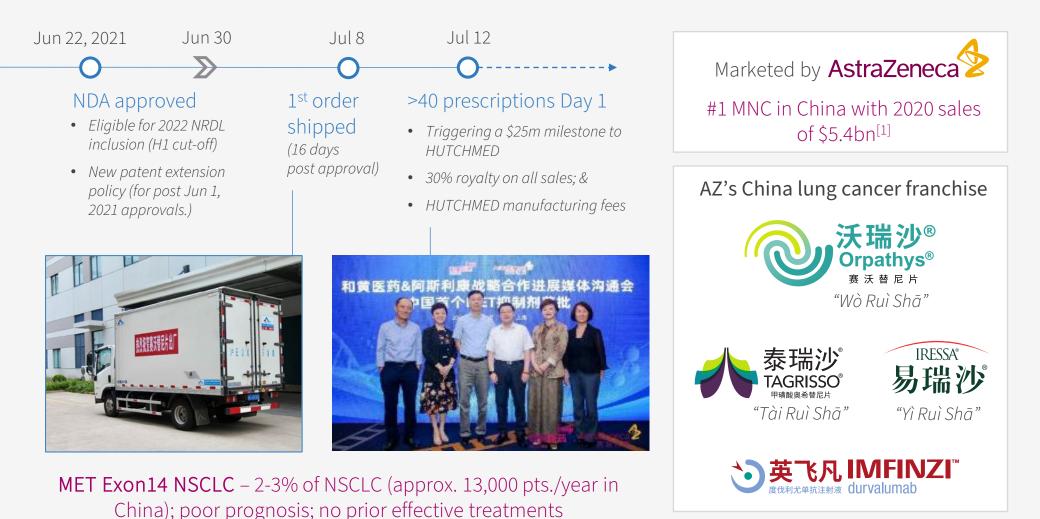


#### H1 2021 commercial activities

- ~34,000 new China pts/yr. with advanced NET
- Launch campaign of local, regional & national events involving ~12,000 HCPs
- Early Access & Patient Access Programs led to use by over 2,000 patients
- Evaluating long term pricing strategy: 2022 NRDL vs. current pricing & access programs
- 30+ exploratory studies including IITs in a broad range of indications – expanding awareness of SULANDA<sup>®</sup> in China

# **ORPATHYS<sup>®</sup> China's first selective MET inhibitor HUTCHMED**

# First indication approved globally: MET Exon 14 skipping NSCLC



# **ORPATHYS<sup>®</sup> efficacy in NSCLC, Gastric & PRCC**

# ...and 5 registration studies set to start in H2 2021



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SUBSTA		UBLISHED DATA	
ıdy	Journal / Meeting	Primary efficacy	
<b>/OIR</b> vo mono)	JAMA Oncology	ORR: 27% vs. 7% (Sutent) PFS: 7.0mo vs 5.6mo (Sutent) OS: NC vs. 13.2mo (Sutent) [HR=0.51, 95% CI: 0.21-1.17] ORR: 57% in MET-driven OS: 27.4mo in MET-driven	
<b>LYPSO</b> vo + IMFINZI®)	ASCO20 Virtual		
<b>TON</b> /0 +	THE LANCET Oncology	<b>ORR:</b> 33-67% <b>PFS:</b> 5.5-11.1BD	
GRISSO®) March TORY vo mono)	(100) 2020 World Conference on Lung Cancer Singapore	<b>ORR:</b> 50% in MET amp	
ET ex14 NSCLC	THE LANCET Respiratory Medicine ASCO20 Virtual	<b>ORR:</b> 42.9%	

# **ORPATHYS<sup>®</sup>** building blocks



... for major global market potential

		Est	. Annual	Incidend	e ('000) [1	, 2, 3]	Median
		China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[4]</sup>
沃瑞沙 <sup>®</sup> Orpathys <sup>®</sup> <sub>赛沃替尼片</sub>	Colorecta MET+ EGFR r	4	3	3	1	11	TBD
赛沃替尼片	<b>Esophageal</b> MET Gene Ampl.	16	1	1	1	20	TBD
	<b>Gastric</b> Gene Ampl.	24	1	3	7	35	<b>8.0 mo.</b> VIKTORY Ph.II
<b>PRCC</b> <i>MET positive</i>		4	4	4	1	14	<b>7.0 mo.</b> SAVOIR Ph.III
<b>NSCLC</b> <i>MET+ EGFR TKI</i> <i>refractory (3<sup>rd</sup> gen.)</i>		21 <sup>[5]</sup>	7	4	7	40	<b>5.4 mo.</b> TATTON Ph.II
<b>NSCLC</b> MET+ EGFR TKI refractory (1 <sup>st</sup> /2 <sup>nd</sup> gen.)		12	3	2	3	20	<b>9.0 mo.</b> TATTON Ph.II
<b>NSCLC</b> <i>MET Gene Ampl.</i>		26	7	7	4	44	TBD
NSCLC MET Exon14d		13	5	5	3	26	<b>8.3 mo.</b> Registr. Ph.II
		120	32	30	28	210	
[1] Globocan; [2] SEER; [3] Company estimates;		ration Stu nning for 2				C & only tr alternativ	

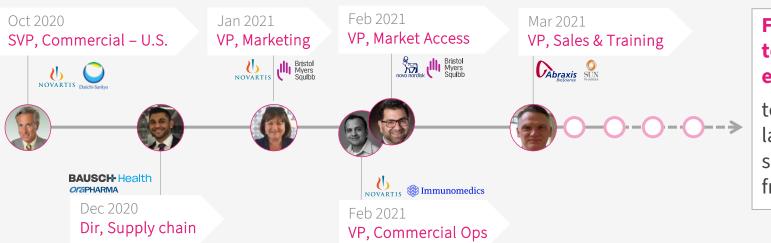
[4] DOT = duration of treatment in latest study; [5] In 2020, TAGRISSO® treated approximately 20k patients. With NRDL inclusion and 64% price reduction, we estimate TAGRISSO® is likely to treat approximately 60k patients.

# **U.S. commercial organization**



# Building on a strong clinical & regulatory team

#### Experienced functional leads in place for commercialization – fully engaged on all aspects of launch readiness



#### Full commercial team in place by early 2022

to support potential launches of surufatinib in 2022 & fruquintinib in 2023

In collaboration with an established international clinical & regulatory functions

Regulatory Affairs						Medic	al Affairs	
Clinical Development & Operations				Quality & Safety				
Surufatinib	Fruquintinib	Europe	Early Stage Assets		Clinical Pharmacology	Product Safety & Pharmaco- vigilance	Quality Assurance & Compliance	Non-Clinical Safety & Toxicology



# **3. CLINICAL DEVELOPMENT UPDATES**

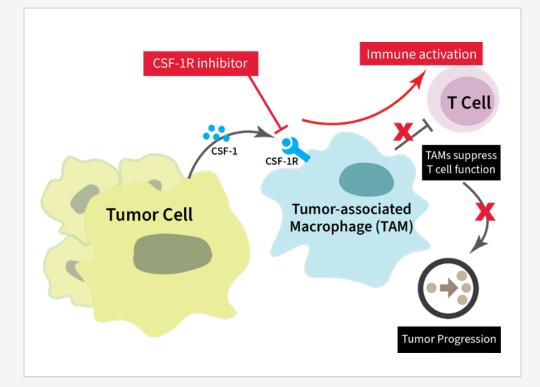
# Surufatinib recap: Unique MOA differentiation HUTCHMED

Potentially enhance immune-mediated anti-tumor effect in addition to anti-angiogenesis

Inhibits VEGFR1/2/3 & FGFR1 – blocking vascular cell growth & angiogenesis

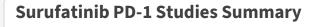
Inhibits CSF-1R – limits production of TAMs which cloak the cancer cell from T-cell attack

**Synergistic effect with PD-1 inhibitors** (AACR 2020, ASCO 2021)



# **Surufatinib: Promising PD-1 combos**

# Planning first Phase III in China in ≥2L NEC with Junshi; additional registration studies under discussion



PD-1	Patient focus		Status/ plan
TUOYI®	NEC ASCO	CN	
TUOYI®	Biliary tract	CN	
TUOYI®	Gastric Asco	CN	Phase II ongoing
TUOYI®	Thyroid	CN	
TUOYI®	Small cell lung	CN	Total N~250
TUOYI®	Soft tissue sarcoma	CN	to select 1-3 for registration
TUOYI®	Endometrial	CN	intent studies
TUOYI®	Esophageal	CN	
TUOYI®	NSCLC	CN	
TYVYT®	Solid tumors	CN	Phase I dose escalation completed
Tisle- lizumab	Solid tumors	US EU	Phase I/Ib ongoing
			Total N~110

ABSTRACT	Surufatinib + toripalimab <sup>[1]</sup>	Surufatinib + toripalimab <sup>[2]</sup>	Lenvatinib + pembrolizumab <sup>[3]</sup>
Indication	Neuroendocrine Carcinoma (2L)	Gastric or GEJ (2L)	Gastric or GEJ (2L)
Efficacy evaluable	20	15	26
Duration of tx, mo. [DCO]	5 [Dec 31, 2020]	3 [Dec 31, 2020]	7 [Apr 10, 2020]
ORR	20.0% [5.7 – 43.7]	Confirmed: 13.3% [1.7 – 40.5]	11.5%
DCR	70% [45.7 - 88.1]	73% [44.9 – 92.2]	58%
mPFS, mo.	3.9 [1.3 – NR]	3.7 [1.41 – NR]	2.5 [1.8-4.2]
mOS, mo.	Not mature at DCO	Not mature at DCO	5.9 [2.6-8.7]



# Surufatinib: Development summary



# Current development status and next steps

#### CHINA

#### Extra-pancreatic (non-pancreatic) NET

- NDA approved Dec 2020
- Launched Jan 2021
- Evaluating long term pricing strategy

#### Pancreatic NET

- Recommended in China Medical Association guidelines in May 2021
- NDA approved June 2021

#### PD-1

- NEC: preparing to initiate Phase III
- Gastric / GEJ: registration design under discussion
- BTC & 6 other cohorts: data continuing to mature
- 30+ exploratory studies ongoing, including IITs

#### GLOBAL

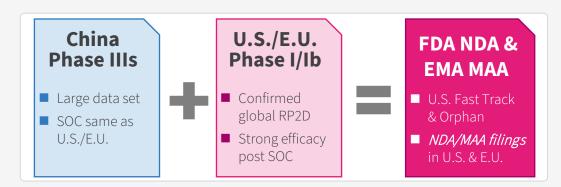
#### U.S. FDA NDA accepted June 2021

- Fast Track Designations for both pNET & non-pNET
- Orphan Drug designation granted for pNET
- PDUFA date April 30, 2022

# EMA MAA submitted and accepted July 2021 Japan registration path agreed with PMDA

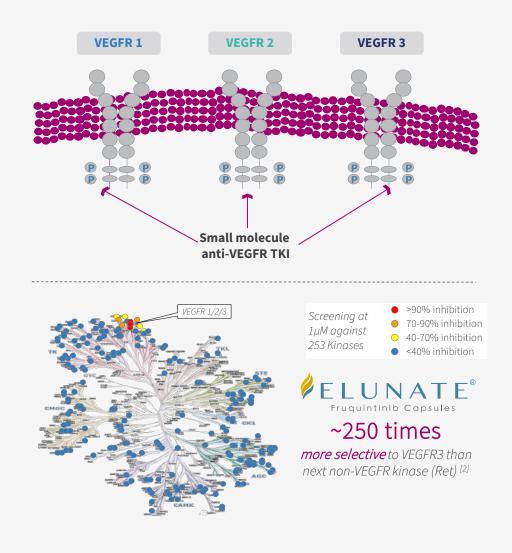
#### PD-1 combinations with tislelizumab in U.S. & E.U.

• CRC, NET, SCLC, gastric, STS cohorts planned: FPI March 2021



# Fruquintinib recap: 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

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- **Highly selective** vs. other kinases with good safety profile with readily manageable AEs
- Combinable with chemo, targeted therapies and IO

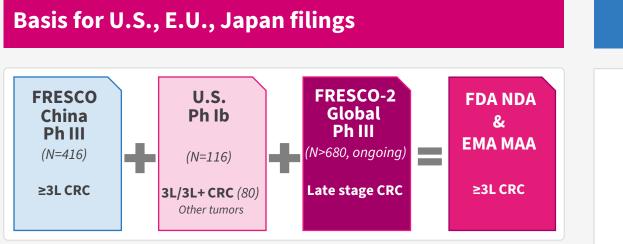
3 <sup>rd</sup> -Line Metastatic Colorectal Cancer	FRESCO Phase III			
Treatment arms	<b>ELUNATE</b> ®	Placebo		
≥G3 AE (Safety population)	61.1%	19.7%		
VEGFR on-target related AEs $\geq$ G3:				
Hypertension	21.2%	2.2%		
Hand-Foot Syndrome	10.8%	0.0%		
Off-target (i.e. non-VEGFR) related AEs	≥ G3:			
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:	i		
ALT increased	0.7%	1.5%		
AST increased	0.4%	0.7%		
Blood bilirubin increased	1.4%	1.5%		

# FRESCO-2 to support 3L+ mCRC U.S./E.U./JP NDA



#### NDA Pogulatory

Regulatory alignment on fruquintinib across all major markets

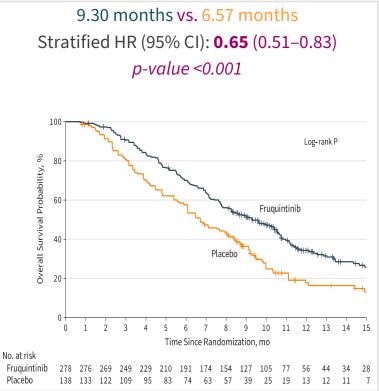


 Target Patient Population – We are aiming for aggregate clinical data to support U.S. NDA & E.U. MAA in third-line and above metastatic CRC

# • FRESCO-2 Global Ph.III

- Enrolling >150 sites across 14 countries
- Target fully enrolled end of 2021
- U.S. Fast Track designation → potential for rolling submission
- Extensive list of supportive studies

# FRESCO China Ph.III (≥3L CRC):



# Fruquintinib: PD-1 inhibitor combinations

# Durable benefit seen in advanced colorectal cancer

Fruquintinib PD-1 studies Summary						
PD-1	Patient focus		Status/ plan			
TYVYT®	CRC	CN	Phase II ongoing Est. N~35			
TYVYT®	Hepatocellular carcinoma	CN	Phase Ib/II ongoing;			
TYVYT®	Endometrial cancer	CN	Total est. N~120			
TYVYT <sup>®</sup>	RCC	CN	registration intent			
TYVYT <sup>®</sup>	Other GI	CN	studies			
Tislelizumab	TNBC	US	Phase I/Ib In planning Est. N~80			
Tislelizumab	Solid tumors	TBD	Phase I/Ib In planning Est. N~60+			
Geptanolimab	CRC	CN	Phase Ib ongoing Est. N~15			
Geptanolimab	NSCLC	CN	Phase Ib ongoing Est. N~15			

		ASCO	ASCO	ANNUAL MEETING
ABSTRACT	Fruq mono Ph. III (FRESCO)	Fruq + sintilimab <sup>[1]</sup>	Fruq + geptano- limab <sup>[2]</sup>	Lenvatinib + pembro- lizumab <sup>[3]</sup>
Prior lines of tx	≥2	≥2	67% ≥2	94% ≥2
RP2D VEGFRi dose (n)	5mg QD 3w/1w <i>(278)</i>	5mg QD 2w/1w <i>(22)</i>	4mg QD 3w/1w <i>(15)</i> <sup>[4]</sup>	20mg QD <i>(32)</i>
Data cut-off	Jan 17, 2017	Apr 7, 2021	Dec 15, 2020	Apr 10, 2020
ORR	4.7% [2.1-7.2]	27.3% [10.7-50.2]	26.7%	21.9% [9.3-40.0]
DCR	62.2% [56.3-68.0]	95.5% [77.2-99.9]	80%	46.9% [29.1-65.3]
mPFS, months	3.7 [3.7–4.6]	6.9 [5.4-8.3]	7.3 [1.9-NR]	2.3 [2.0-5.2]
OS, months	9.3 [8.2–10.5]	11.8 <i>[8.8-NR]</i>	Not mature at DCO	7.5 (3.9-NR)

HUTCH

2021 ASCO

[1] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr 2514) data in patients dosed with RP2D; [2] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr e15551) data in 15 ITT patients, of which 6 were dosed with RP2D; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; ab

# **Fruquintinib: Development summary**



# Current development status and next steps

#### CHINA

#### FRUTIGA: Phase III in 2L gastric cancer ongoing

- Expect fully enrolled around YE 2021
- Top-line data expected H2 2022

#### PD-1

- CRC: data promising, registration strategy being formulated
- EMC: registration study under discussion with CDE, expect to initiate H2 2021
- HCC and RCC: registration plans currently under discussion with PIs
- 3 new cohorts added and are enrolling
- 20+ exploratory studies ongoing, including IITs

#### GLOBAL

#### **Colorectal cancer**

- FRESCO-2 Phase III initiated in U.S., E.U. & Japan
- U.S. Phase Ib/II completed
- Basis for U.S., E.U. Japan NDA clear
  - Support for U.S. NDA in third-line and above mCRC

#### **PD-1** combinations

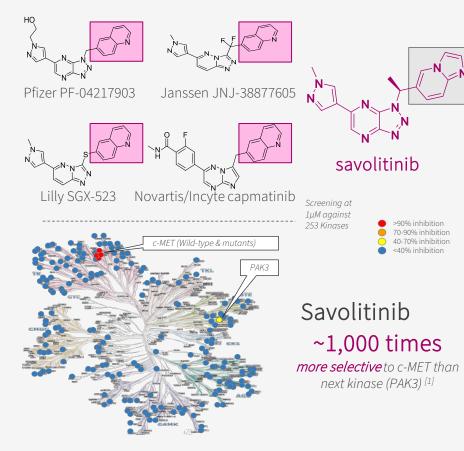
• Ongoing proof-of-concept studies across multiple cohorts, led by both HUTCHMED and BeiGene

# Savolitinib recap: MoA and data summary



# Designed to avoid known renal toxicity while retaining potency

Quinolinone metabolite in 1<sup>st</sup>-gen MET compounds has low solubility in humans and when metabolized by the kidneys, appeared to crystallize, resulting in obstructive toxicity.



# **Evidence of clinical differentiation**

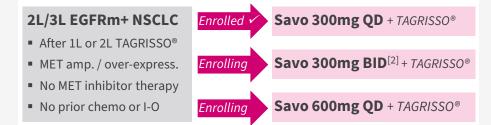
- ~1,200 patients in clinical trials to date
- Competitive anti-tumor effect across multiple MET aberrations in multiple tumor types
- Single agent and combination settings
- First-in-class in China
- Currently testing in multiple tumor types:
  - NSCLC with MET Exon14 skipping
  - EGFRm + NSCLC
  - MET-driven PRCC
  - MET amplified GC

# EGFR TKI refract. NSCLC w/ MET amplification HUTCHM

# Phase III registration studies are being planned in combinations with TAGRISSO® (osimertinib)

wc				
	Savo e	TATTON D Savo 300mg + TAGRISSO®		
	<b>B1</b> Prior 3 <sup>rd</sup> -gen EGFR-TKI	<b>B2</b> No prior 3 <sup>rd</sup> – gen EGFR-TKI (T790M neg.)	<b>B3</b> No prior 3 <sup>rd</sup> -gen EGFR-TKI (T790M pos.)	<b>D</b> No prior 3 <sup>rd</sup> -gen EGFR-TKI (T790M neg.)
<b>ORR</b> *, %	<b>33%</b>	<b>65%</b>	<b>67%</b>	<b>62%</b>
[95% CI]	[22–46]	[50–78]	[41–87]	[46–76]
<b>DCR</b> <sup>#</sup> , %	<b>75%</b>	<b>88%</b>	<b>100%</b>	<b>93%</b>
[95% CI]	[64–85]	[76–96]	[81–100]	[81–99]
<b>Median DoR</b> ,	<b>9.5</b>	<b>10.7</b>	<b>11.0</b>	<b>9.7</b>
mo. [95% Cl]	[4.2–14.7]	[6.1–14.8]	[2.8-NR]	[4.5–14.3]
<b>Median PFS</b> ,	<b>5.5</b>	<b>9.1</b>	<b>11.1</b>	<b>9.0</b>
mo. [95% CI]	[4.1–7.7]	[5.5–12.8]	[4.1–22.1]	[5.6–12.7]

# SAVANNAH: Broadest TAGRISSO<sup>®</sup> refractory population – FISH+ and/or IHC+ line agnostic



#### TO FINALIZE FOR GLOBAL PHASE III

- Dose regimen
- Target patient population
- Diagnostics tools
  - FISH / IHC

# Data will inform global Phase III design

#### Intention to initiate late 2021

[1] Most pts enrolled to Part B1, B2, B3 on 600 mg savolitinib; final 21 patients enrolled in Part B were dosed with savolitinib by body weight following a protocol amendment, as follows: pts  $\leq$ 55 kg (n=8) 300mg daily, pts >55 kg (n=13) 600mg daily. Best response data are for patients who had an opportunity to have two follow-up scans; \* Complete or partial response confirmed at  $\geq$ 4 weeks. # Disease control rate = confirmed complete response + confirmed partial response + stable disease at  $\geq$ 5 wks; CI, confidence interval; NR, not reached. Han JY, et al. Osimertinib + savolitinib in patients with EGFRm MET-amplified/overexpressed NSCLC: Phase Ib TATTON Parts B and D final analysis. WCLC January 2021 #FP14.03.

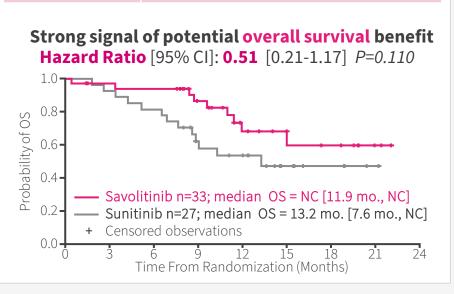
# Savolitinib: Promising in MET-driven PRCC

# Global Phase III trial in planning in combination with IMFINZI<sup>®</sup> (durvalumab)



HUTCH

# SAVOIR: Single agent anti-tumor activity in MET-driven PRCCAll 9 savo responders remained in response at data cut-offSAVOIR [1]Savolitinib (N=33)Sunitinib (N=27)ORR\* [95% CI]27% [13.3-45.5]7% [0.9-24.3]PFS [95% CI]7.0 mo. [2.8-NC]5.6 mo. [4.1-6.9]Hazard Ratio: 0.71 [0.37-1.36]



#### Highly correlated to MET-driven alterations / amplif. 57% ASC 29% MET DNA alterations (central analysis: chromosome 7 gain / MET or HGF amplification, kinase domain mutations) All patients (12/41) MET-driven (8/14) All patients (N=41) MET-driven (N=14) ORR 29% 57% 4.9 mo. [2.5-10.0] mPFS 10.5 mo. [2.9-15.7] mOS 14.1 mo. [7.3-30.7] 27.4 mo. [7.3-NR] PFS @ 12 mo. 29.6% [16.1-44.3] 46.2% [19.2-69.6] 64.3% [34.3-83.3] OS @ 12 mo. 54.3% [37.5-68.4]

CALYPSO: IMFINZI<sup>®</sup> (PD-L1i) combination activity<sup>[2]</sup>

\*1 of 2 sunitinib responders remained in response at data cut-off. NC = not calculated.

[1] Choueiri TK, et al. Efficacy of Savolitinib vs Sunitinib in Patients With MET-Driven Papillary Renal Cell Carcinoma: The SAVOIR Phase 3 Randomized Clinical Trial. JAMA Oncol. Published online May 29, 2020. doi:10.1001/jamaoncol.2020.2218; [2] ASCO 2021 Suárez C et al. J Clin Oncol 39, 2021 (suppl 15; abstr 4511).

# Savolitinib development summary



#### CHINA

#### MET Exon14 skipping NSCLC

- NDA approved in June 2021
- Commercialized by AstraZeneca
- Present in other tumor types: Secondary GBM, GI tumors, Histiocytic sarcoma

# 2L EGFR TKI refractory NSCLC with MET amplification

- Savolitinib + TAGRISSO<sup>®</sup> Phase III registration study
- FPI expected late H2 2021 **SACHI Study**

#### 1L EGFRm+ NSCLC with MET overexpression

- Savolitinib + TAGRISSO<sup>®</sup> Phase III registration study
- FPI expected late H2 2021 **SANOVO Study**

#### Gastric cancer with MET amplification

- Single arm study with potential for registration
- FPI in July 2021

#### GLOBAL

## **MET-driven PRCC**

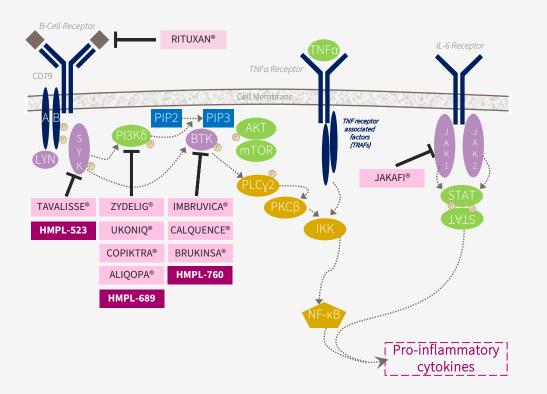
- Phase III registration study
- Savolitinib + IMFINZI® vs. sunitinib in MET-driven PRCC
- Expected study initiation H2 2021
   SAMETA Study

# 2L TAGRISSO<sup>®</sup> refractory NSCLC with MET amplification

- Savolitinib + TAGRISSO<sup>®</sup> Phase III registration study
- FPI expected late YE 2021

# HMPL-689 recap: Highly selective PI3Kδ inhibitor HUTCHMED

First in our next wave of innovation targeting B-cell signaling pathway



# B-cell signaling is critical in hematological cancer

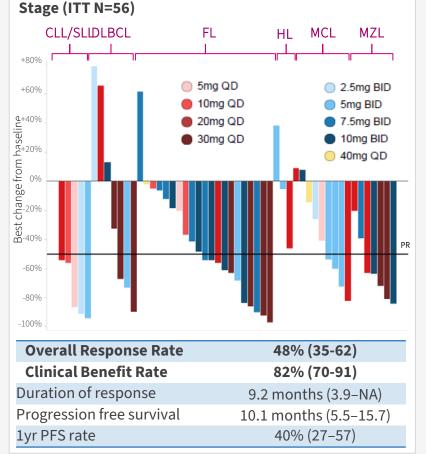
# Designed to be a global best-in-class inhibitor of $\text{PI3K}\delta$

- Improved isoform selectivity (sparing PI3Kγ)
- Improved potency at whole blood level (>5x more potent than Zydelig) to cut compound related toxicity
- Improved PK particularly efflux and drug/drug interaction due to CYP inhibition / induction, critical for combos

Enzyme IC₅₀ (nM)	HMPL-689	ZYDELIG®	COPIKTRA®	ALIQOPA®
ΡΙ3Κδ	0.8	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 <b>(142x)</b>	104 <b>(52x)</b>	2 <b>(2x)</b>	6.4 <b>(9x)</b>
PI3Kα (fold vs. PI3Kδ)	>1,000 (>1,250x)	866 <b>(433x)</b>	143 <b>(143x)</b>	0.5 <b>(1x)</b>
ΡΙ3Κβ (fold vs. ΡΙ3Κδ)	87 <b>(109x)</b>	293 <b>(147x)</b>	8 <b>(8x)</b>	3.7 <b>(5x)</b>
PI3Kδ human <u>whole</u> <u>blood</u> CD63+	3	14	15	n/a

# HMPL-689: initiated registration-intent trial

Promising activity in multiple tumors, with advantages in tolerability versus PI3Kδ inhibitors More data gathered since ASH dose escalation data cut-off (Sep 2020) to be presented



**Best Response of Target Lesions in Dose Escalation** 

Incidence of select treatment emergent adverse events – all AEs / grade ≥3 AEs

HUTCHM

	HMPL- 689 <sup>[1]</sup>	<b>Zydelig®</b> (idelalisib) <sup>(2)</sup>	<b>Aliqopa®</b> (copanlisib) <sup>(2)</sup>	<b>Copiktra®</b> (duvelisib) <sup>[2]</sup>	<b>Ukoniq®</b> (umbralisib) <sup>[2]</sup>	Parsaclisib (Dose escalation) <sup>(</sup> 3)	Parsaclisib (CITADEL-204/ MZL) <sup>(4)</sup>	Zandelisib (intermittent dosing) <sup>(5)</sup>	Zandelisib (Dose escalation) <sup>(6)</sup>
n	56	146	168	442	221	72	100	21	30
Neutropenia	43% / 11%	53% / <b>25%</b> *	32% / <b>25%</b>	34% / <b>30%</b>	33% / 16%*	44% / <b>20%</b> *	13% / 9%	na / 14%	45% / 13%*
Anemia	16% / 0%	28% / 2%*	na	20% / 11%	27% / 3%*	31% / 8%*	14% / 5%	na / 0%	13% / 0%*
Thrombocytop enia	11%/0%	26% / 6%*	22% / 8%	17% / 10%	26 % / 4%*	35% / 10%*	na	na / 0%	22% / 0%*
Diarrhea or colitis	<5% / <5%	47% / 14%	36% / 5%	50% / 23%	58% / 10%	36% / 9%	<b>44% / 11%</b>	na / 4%	45% / 19%
Rash	11% / 5%	21% / 3%	15% / 2%	31% / 9%	18% / 3%	31% / 6%	17% / 2%	na / 2%	42% / 13%
ALT increased	27% / 2%	50% / <b>19%</b>	na	40% / <mark>8%</mark>	33% / <mark>8%</mark>	28% / 1%	26% / 4%	na / 0%	39% / <b>6%</b>
AST increased	21% / 2%	41% / <b>12%</b>	na	37% / <b>6%</b>	32% / <b>7%</b>	29% / 1%	19% / 2%	na / 0%	25% / <mark>6%</mark>
Pyrexia	14% / 0%	28% / 2%	na	26% / 2%	na	18% / 1%	13% / 1%	na	na
Pneumonia	25% / 16%	25% / 16%	21%/ 14%**	21%/15%	PJP prophylaxis recommended	na	7% with PJP prophylaxis	PJP prophylaxis	na
Hypertension	7% / 5%	na	35% / 27%	na	na	7% / 0%	na	na	na
Hyperglycemia	11% / 2%	na	54% / 39%	na	na	10% / 1%	na	na	na

CLL/SLL: chronic lymphocytic leukemia/small lymphooxytic lymphoma; **FL**: follicular lymphoma; **MZL**: marginal zone lymphoma; **MCL**: mantle cell lymphoma; **DLBCL**: diffuse large B cell lymphoma; **HL**: Hodgkin's lymphoma; **IV**: non-Hodgkin's lymphoma. NE: 2 DLBCL pts EOT due to AE (5mg BID) & voluntary withdraw (7.5 mg BID); 1 FL pt EOT due to AE (20 mg QD) before 1<sup>st</sup> tumor evaluation. 1 CLL arrive PR based on target lesion, as lymphocyte cell count increased assessed PD at C3D1. [1] ASH 2020 Abstract #135; [2] US Prescribing Information; [3] ASCO 2019 Abstract #7506; [4] ASH 2020 Abstract #2934; [5] Blood, April 2019 doi: 10.1182/blood-2018-08-867499; [6] ] ASH 2020 Abstract #338; [7] ASCO 2020 Abstract #8016; [8] ASCO 2018 Abstract #7519; \*Laboratory values; \*Lower respiratory tract infections; \*\* Regardless of causility; PJP = pneumocystis jirovecii pneumonia

# HMPL-689: Development summary and registration pathway



#### CHINA

#### Monotherapy

- FL / MZL registration study started April 2021
  - NDA submission potentially late 2022 / early 2023
- Additional indications will be planned

#### Combinations

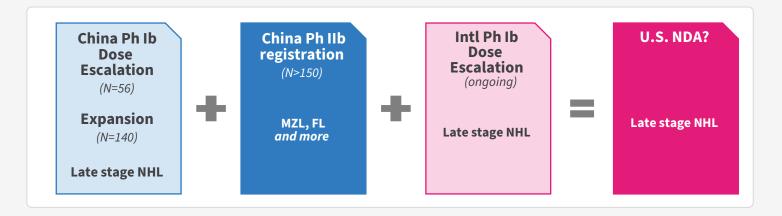
- Additional indications
- Earlier lines
- To start in early 2022

#### GLOBAL

# U.S. & E.U. Ph.I multiple dose cohorts complete

#### Next steps

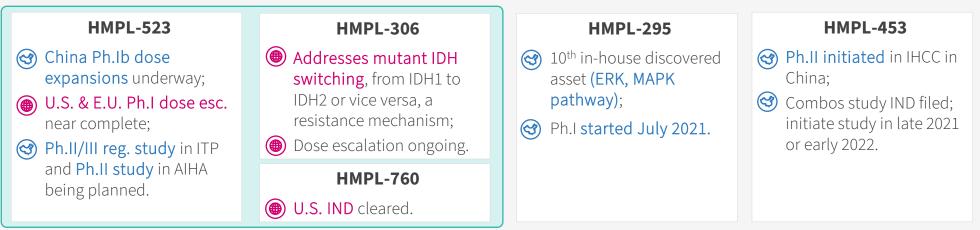
- Evaluate efficacy signals using cumulative HMPL-689 data from both International and China studies, and RP2D selection
- Engage FDA in late 2021 through End of Phase 1 meeting to confirm registrational path



# Next wave of innovation



#### Hematological malignancies assets



Program	Treatment	Target Patient	Sites	Dose Finding / Safety Run-in	Proof-of-concept	Registration	
	HMPL-523	Indolent NHL	US/EU/AU				
HMPL-523	HMPL-523	B-cell malignancies	China				
Syk	HMPL-523	ITP	China				
	HMPL-523	AIHA	China		*		
<b>HMPL-453</b> FGFR 1/2/3	HMPL-453	IHCC	China				
HMPL-306 IDH 1/2	HMPL-306 HMPL-306	Hematological malignancies Hematological malignancies & solid tumors	China US/EU				
HMPL-295 (ERK, MAPK pathway	HMPL-295	Solid tumors	China				
HMPL-760 (BTK, 3G)	HMPL-760 HMPL-760	Hematological malignancies Hematological malignancies	US/EU China	*			



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# 4. POTENTIAL UPCOMING CLINICAL & REGULATORY EVENTS

# **Potential upcoming events**



# Clinical & regulatory milestones in U.S., E.U. & Japan

				Early '21	Mid '21	Late '21	2022
Surufatinib (VEGFR 1/2/3; FGFR1; & CSF-1R inhibitor)	NETs mono.	NDA	U.S. NDA submission	$\checkmark$			
	Solid tumors	Ph. lb/lls	Tislelizumab PD-1 combo start	$\checkmark$			
	NETs mono.	MAA	E.U. MAA submission**		$\checkmark$		
	NETs mono.	Market	U.S. NDA & E.U. MAA approval and launch				۲
	TNBC PD-1 combo	Ph. lb/lls	Tislelizumab PD-1 combo start		C	<b>)</b>	
Fruquintinib	CRC mono	Ph. III	FRESCO-2: Recruitment completion			0	
(VEGFR 1/2/3 inhibitor)	CRC mono	Ph. Ib	Data at a scientific conference*				0
	CRC mono	Ph. III	FRESCO-2: Readout & NDA subm.***				۲
	PRCC PD-L1 combo	Ph. II	CALYPSO: IMFINZI® combo data (ASCO)	$\checkmark$			
Savolitinib (MET inhibitor)	PRCC PD-L1 combo	Ph. III	SAMETA: IMFINZI® combo start**		6	Ð	
	EGFR-TKI refract., MET+ NSCLC	Ph. III	EGFR combo (TAGRISSO®) start**			۲	
<b>HMPL-689</b> (ΡΙ3Κδ inhibitor)	Hematological malignancies	Ph. Ib	Expansion start***		0		
	nematological malignaticles		Regulatory dialogue**			0	
HMPL-523 (Syk inhibitor)	Uppentale gigal maligner aging	Ph. Ib	Expansion start***		C	C	
	Hematological malignancies	Ph. Ib	Escalation data at scientific conf.*			0	
HMPL-306 (IDH1/2 inhibitor)	Hematological malignancies &	Ph.I	Start	✓			
	solid tumors	Ph.I	Complete dose escalation and start expansion			C	)
HMPL-760 (covalent BTK inhibitor)	Hematological malignancies	Ph.I	Start**			C	)
New assets	_	-	IND filings***			C	)

\* Subject to acceptance by scientific conference; \*\* subject to regulatory interaction; \*\*\* subject to supportive data. Bold = regulatory progress or new clinical data.

# **Potential upcoming events**



# Clinical & regulatory milestones in China

				Early '21	Mid '21	Late '21	2022
Surufatinib (VEGFR 1/2/3; FGFR1; & CSF-1R inhibitor)	non-pNET & pNET	Market	Approval & launch	$\checkmark$	$\checkmark$		
	NEC & GC PD-1 combo	Ph. lb/ll	TUOYI <sup>®</sup> PD-1 combo data (ASCO)	$\checkmark$			
	Further PD-1 combo	Ph. Ib/II	Data at a scientific conf.*			0	
CSF-IR IIIIIDILOI)	PD-1 combo	Ph. II	Registration intent study start**			0	
Fruquintinih	CRC PD-1 combos	Ph. lb/ll	TYVYT <sup>®</sup> & geptano. combos data (ASCO)	$\checkmark$			
	Further PD-1 combo	Ph. Ib/II	Data at a scientific conf.*			0	
Fruquintinib (VEGFR 1/2/3 inhibitor)	PD-1 combo	Ph. II	Registration intent study start**			0	
(VEGI (1)2)0 minorcoly	GC paclitaxel combo	Ph. III	FRUTIGA: recruitment completion			0	
	GC paclitaxel combo	Ph. III	FRUTIGA: readout & NDA submission***				۲
	MET Ex14 skipping NSCLC	Market	Approval & launch by AZ		$\checkmark$		
Savolitinib	MET+GC	Ph. II	Registration potential study start		$\checkmark$		
(MET inhibitor)	EGFR-TKI refract., MET+ NSCLC	Ph. III	SACHI: TAGRISSO <sup>®</sup> combo start**			$\bigotimes$	
	EGFRm+, MET+ NSCLC	Ph. III	SANOVO: TAGRISSO <sup>®</sup> combo start**			$\bigotimes$	
	NHL multiple subtypes	Ph. II	Registration intent studies start **	$\checkmark$			
HMPL-689 (PI3Kδ inhibitor)	NHL multiple subtypes	Ph. lb	Expansion data at a scientific conf.*			€	
	NHL multiple subtypes	Ph. Ib	Initiate combo studies**				0
	AIHA	Ph.II	Start**			0	
HMPL-523 (Syk inhibitor)	ITP	Ph. Ib	Data at a scientific conf.*			0	
(Syx IIIIIDICOI)	ITP	Ph. III	Start**			0	
HMPL-453 (FGFR 1/2/3i)	Solid tumors	Ph. Ib	Initiate combo studies**			C	)
HMPL-306 (IDH 1/2i)	Hematological malignancies	Ph.I	Complete dose escalation and start expansion			C	)
HMPL-295 (ERKi)	Solid tumors	Ph.I	Start		$\checkmark$		
HMPL-760 (covalent BTKi)	Hematological malignancies	Ph.I	Start**			0	
New assets	_	-	IND filings***			C	)

\* Subject to acceptance by scientific conference; \*\* subject to regulatory interaction; \*\*\* subject to supportive data. Bold = regulatory progress or new clinical data.

### 2021: Another busy year for HUTCHMED



10 new registration studies	Savolitinib: 5	<ul> <li>2L EGFR TKI refractory NSCLC, China; 2L EGFR TKI refractory NSCLC, global; 1L EGFRm+ with MET overexpression, China; MET driven PRCC, global; MET amplified GC</li> </ul>
	Surufatinib: 1	<ul> <li>2L NEC, in combination with TUOYI<sup>®</sup></li> </ul>
	Fruquintinib: 1	• 2L EMC, in combination with TYVYT®
	HMPL-689: 2	• 2L MZL; 3L FL
	HMPL-523: 1	• ITP
	HMPL-760	• Third generation BTK inhibitor: U.S., China
3 new INDs	HMPL-653	CSF-1R inhibitor: China
	HMPL-A83	• CD47 monoclonal antibody: U.S., China



### **5. FINANCIALS & SUMMARY**

### **Condensed Consol. Balance Sheet**



#### (in US\$'000)

	Dec 31,	Jun 30,
	2020	2021
Assets		(Unaudited)
Cash, cash equivalents & short-term investments	435,176	950,448
Accounts receivable	47,870	58,878
Other current assets	47,694	81,848
Property, plant and equipment	24,170	29,168
Investments in equity investees	139,505	118,316
Other non-current assets	29,703	34,231
Total assets	724,118	1,272,889
Liabilities and shareholders' equity		
Accounts payable	31,612	28,513
Other payables, accruals and advance receipts	120,882	181, 610
Bank borrowings	26,861	26,883
Other liabilities	25,814	22,188
Total liabilities	205,169	259,194
Total Company's shareholders' equity	484,116	984,795
Non-controlling interests	34,833	28,900
Total liabilities and shareholders' equity	724,118	1,272,889

### As of Jun 30, 2021 Cash Resources:

- \$950m cash / cash eq. / ST inv. <sup>[1]</sup>
- Not including **additional ~\$250m** in H2 resulting from:
  - \$77m HK IPO over-allotment, net
  - \$25m ORPATHYS® 1st sale milestone
  - ~\$150m non-core OTC divestment

#### H1 2021 Equity Financings:

- \$100m PIPE BPEA (Apr 2021)<sup>[2]</sup>
- \$508m HK IPO (Jun 2021 net pre-O/A)

#### Other:

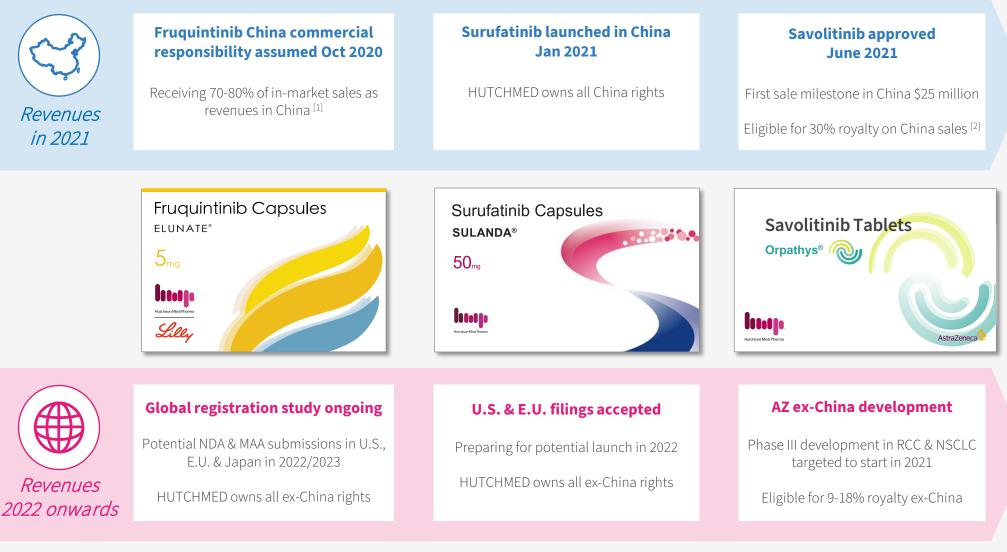
- \$69m unutilized banking facilities [3]
- \$27m in bank borrowings
- \$55m additional cash at SHPL JV

[1] Short-term investments: deposits over 3 months; [2] Private placement to Baring Private Equity Asia. [3] From HSBC & Deutsche Bank.

### 3 novel drugs launched



#### 2021 Oncology consolidated revenues guidance **\$110-\$130 million** (vs. 2020 \$30.2m actual)



[1] In a China collaboration with Eli Lilly, HUTCHMED owns all rights outside of China; [2] To be commercialized by AstraZeneca globally.

### **Condensed Consol. Statement of Operations**

#### (in US\$'000, except share and per share data)

YE Dec 31,	6 Mths End	led Jun 30,
2020	2020	2021
	(unau	
19,953	8,645	37,795
10,262	7,747	5,056
30,215	16,392	42,851
197,761	90,373	114,511
227,976	106,765	157,362
(188,519)	(83,572)	(123,249)
(174,776)	(73,974)	(123,050)
(61,349)	(27,384)	(54,797)
(424,644)	(184,930)	(301,096)
(196,668)	(78,165)	(143,734)
6,934	1,585	3,287
(189,734)	(76,580)	(140,447)
(4,829)	(2,032)	(1,859)
79,046	30,366	42,966
(115,517)	(48,246)	(99,340)
(10,213)	(1,448)	(3,057)
(125,730)	(49,694)	(102,397)
(0.18)	(0.07)	(0.14)
(0.90)	(0.35)	(0.70)
	2020 19,953 10,262 30,215 197,761 227,976 (188,519) (174,776) (61,349) (424,644) (196,668) 6,934 (196,668) 6,934 (189,734) (4,829) 79,046 (115,517) (10,213) (125,730) (0.18)	2020         2020 (unau           19,953         8,645           10,262         7,747           30,215         16,392           197,761         90,373           227,976         106,765           (188,519)         (83,572)           (174,776)         (73,974)           (61,349)         (27,384)           (424,644)         (184,930)           (196,668)         (78,165)           6,934         1,585           (189,734)         (76,580)           (4,829)         (2,032)           79,046         30,366           (115,517)         (48,246)           (10,213)         (1,448)           (125,730)         (49,694)           (0.18)         (0.07)



#### 2021 Guidance

#### \$110-130m in consolidated Oncology/Immunology revenue

- Accelerating growth on ELUNATE®
- Full year sales on SULANDA®
- ORPATHYS<sup>®</sup> 30% royalties, mfg sales & 1<sup>st</sup> sale milestone

Rapid expansion of organization & development on 11 novel oncology candidates – 6 in global development

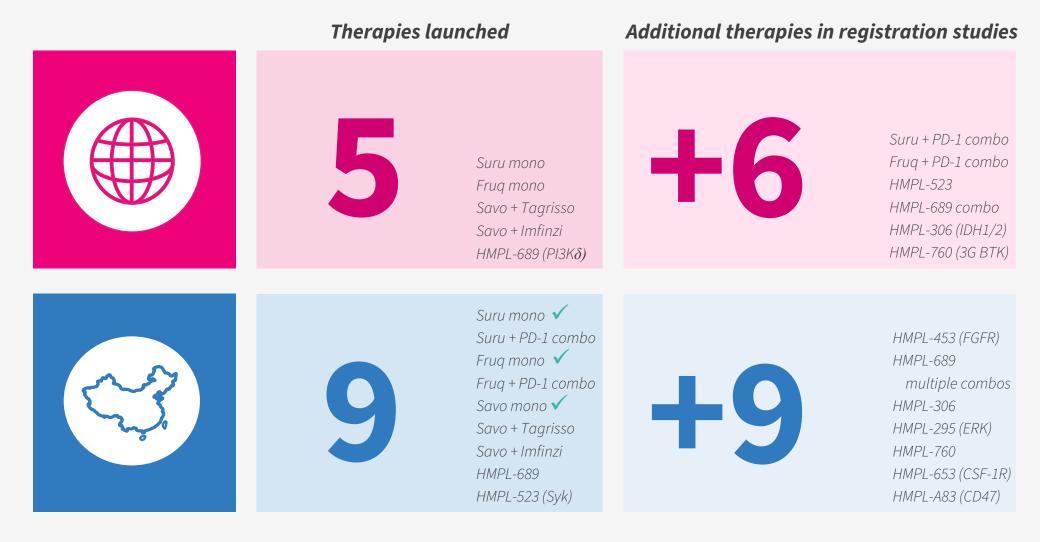
- U.S. & Europe R&D expense grew to \$59.3m in H1 2021 (H1-20: \$19.9m)
- China R&D expense grew to \$63.8m in H1 2021 (H1-20: \$54.1m)

### **HUTCHMED 2025**





#### Ambitious targets with potential for transformation



#### 42

### Thank you



www.hutch-med.com



#### **Estimated Incidence in Main Target Indications**

### 



#### Strategies

- Realizing global potential of novel oncology assets
- Building a fully integrated China oncology business



### **Product Candidate Details**



#### **Commercial Expertise**



#### Manufacturing Expertise



**Further Corporate Information** 

# APPENDIX



### **A1**

### ESTIMATED INCIDENCE IN MAIN TARGET INDICATIONS

### Savolitinib market potential



#### First-in-class selective METi in China – global studies planned in NSCLC & PRCC

	Ũ		Est	Est. Annual Incidence ('000) [1, 2, 3]			Median	
			China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[4]</sup>
		<b>Colorectal</b> MET+ EGFR ref.	4	3	3	1	11	TBD
	<b>Esopha</b> MET Gene		16	1	1	1	20	TBD
	<b>Gastric</b> <sup>-</sup> Gene Ampl.		24	1	3	7	35	<b>8.0 mo.</b> VIKTORY Ph.II
<b>PRCC</b> MET positive		_	4	4	4	1	14	<b>7.0 mo.</b> SAVOIR Ph.III
<b>NSCLC</b> MET+ EGFR TKI refractory (3 <sup>rd</sup> gen.)			21 <sup>[5]</sup>	7	4	7	40	<b>5.4 mo.</b> TATTON Ph.II
<b>NSCLC</b> <i>MET+ EGFR TKI</i> <i>refractory (1<sup>st</sup>/2<sup>nd</sup> gen.)</i>			12	3	2	3	20	<b>9.0 mo.</b> TATTON Ph.II
<b>NSCLC</b> <i>MET Gene Ampl.</i>			26	7	7	4	44	TBD
NSCLC MET Exon14d			13	5	5	3	26	<b>8.3 mo.</b> Registr. Ph.II
			120	32	30	28	210	
[1] Globocan; [2] SEER; [3] Company estimates;	21	in	egistration Stu planning for 2	2021		ć	C & only tr alternative	

[4] DOT = duration of treatment in latest study; [5] In 2020, Tagrisso treated approximately 20k patients. With NRDL inclusion and 64% price reduction, we estimate Tagrisso is likely to treat approximately 60k patients.

### **Fruquintinib market potential**



**Best-in-class selective VEGFRi** – global monotherapy in 3<sup>rd</sup> line CRC; expand through chemo/PD-1 combinations in earlier line settings

				Est. Annual Incidence ('000) <sup>[1, 2, 3]</sup>			2, 3]	Median		
					China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[4]</sup>
		НС	<b>rial TNBC, RCC, C, NSCLC</b> e (+ PD-1 mAb)		TBD	TBD	TBD	TBD	TBD	TBD
	<b>Colorect</b> 2nd Line (+ PD-				165	47	72	44	328	TBD
	<b>Gastric</b> Line (+ Taxol)				234	14	25	68	341	<b>4.0 mo.</b> Ph.Ib study
<b>Colorectal</b> 3rd Line					83	23	36	22	164	<b>4.0 mo.</b> FRESCO Ph.III
					482	84	132	134	832	
[1] Globocan; [2] SEER; [3] Company es	stimates;	Approve	d	Registrat submis	tion Studie sions und	es / NDA erway			-concept s nderway	studies

### Surufatinib market potential



### **Best-in-class VEGFRi with synergistic activity** – global monotherapy in Advanced Grade 1/2 NET; expand through PD-1 combinations in earlier line settings

		Est. Annua			Incidence	Median		
			China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[4]</sup>
	Esophageal, Biliary Tract, SCLC, Gastric, Sarcoma, Thyroid, Endometrial, NSCLC 2nd Line (+ PD-1 mAb)		TBD	TBD	TBD	TBD	TBD	TBD
<b>NET /</b> G3 2nd Line (+			11	8	7	3	29	TBD
<b>Biliary Tract</b> 2nd Line			39	3	3	1	45	TBD
<b>NET</b> Advan. G1/2			34	16	15	6	71	<b>10.0 mo.</b> SANET Ph.IIIs
			84	26	25	10	145	
[1] Globocan; [2] SEER; [3] Company estimates;	Approved	Registrat submis	tion Studie sions und	es / NDA erway			-concept nderway	

### **HMPL-689 market potential**



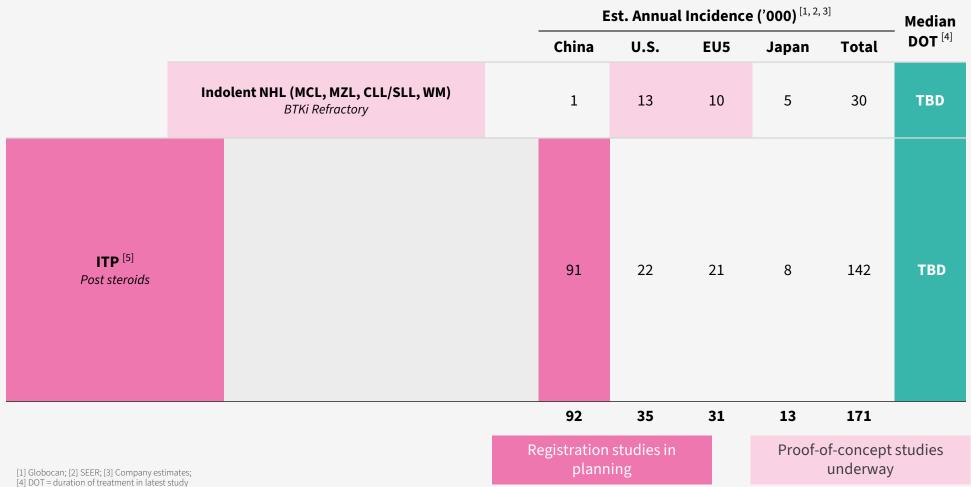
#### **Emerging hematological malignancies asset** – global and China development moving now in parallel in multiple indolent NHL indications

			Est. Annual Incidence ('000) <sup>[1, 2, 3</sup>				2, 3]	Median
			China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[4]</sup>
	iNHL: Diffuse Large B-cell Lymphoma 2nd Line		11	9	8	4	32	TBD
iNH	HL: Mantle Cell Lymphoma 3rd Line		3	3	3	1	10	TBD
iNHL: Marginal Zo Lymphoma 3rd Line				4	4	2	15	TBD
<b>iNHL: Follicular Lymphoma</b> 3rd Line			11	9	9	4	33	TBD
			30	25	23	11	90	
[1] Globocan; [2] SEER; [3] Company estimates;	Registration Studies underway	Re	gistration s planni				-concept : nderway	studies
[4] DOT = duration of treatment in latest study								

### HMPL-523 market potential



**Emerging immunology and hematological malignancies asset** – first approval opportunity in ITP – global opportunity in BTKi refractory indolent NHL



[5] Immune Thrombocytopenic Purpura (prevalence of immune disorder)



## **A2**

### **HUTCHMED STRATEGY**

### **Our Strengths**



#### Fully integrated **1,300+ person** R&D and commercialization platform **built over 20 years**

1	2	3	4
WORLD CLASS DISCOVERY & DEVELOPMENT CAPABILITY	HIGHLY DIFFERENTIATED NME PORTFOLIO & GLOBAL PIPELINE	DEEP PAN-CHINA MARKET ACCESS CAPABILITY	SEASONED MNC MGMT. TEAM – STRONG GOVERNANCE
<b>First</b> global-focused novel drug discovery company in China – established in the early 2000s	<b>10 innovative clinical</b> <b>NMEs</b> – all discovered in-house by HUTCHMED	~ <b>540</b> person oncology team – covering 2,500 China oncology hospitals	<b>11 years</b> – median tenure of 14 person senior mgmt. team
~ <b>720</b> integrated R&D staff focused on oncology & immunological diseases	<b>3 medicines marketed</b> in China – all in advanced global development	Highly profitable Other Ventures with 20-year commercial track record in China	<b>0 governance issues</b> during 14 years as a listed company

### World class discovery engine

#### Most prolific & validated in China biotech

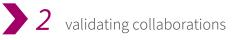
#### Focus on Global Quality Innovation Proven & Validated at All Levels

> 15+ year track record in oncology, fully integrated 700+ person in-house scientific team

**40+** oncology indications in development. 11 TKIs incl. VEGFR, c-MET, PI3Kδ, Syk, FGFR, IDH, ERK and 3G BTK

> 10+ combo therapy trials with chemo, TKI & IO drugs. Superior selectivity enables combos

2 further in-house late pre-clinical molecules

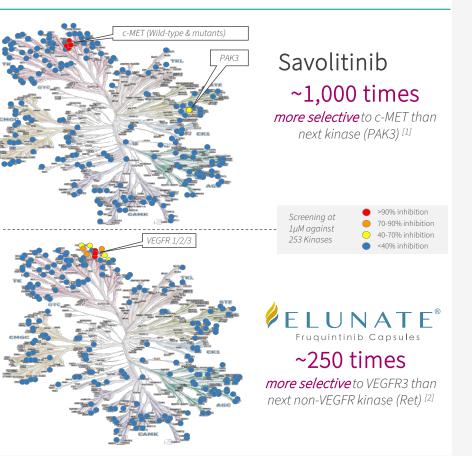


#### AstraZeneca Savolitinib Fri 2011 Global deal 2013

d Fruquintinib 2013 China deal

#### HUTCHMED's Advanced Chemistry Approach Provides Superior Selectivity Profiles

WORLD-CLASS DISCOVERY & DEVELOPMENT CAPABILITY



### **Established global C&R infrastructure**

### Track record of breakthroughs





Integrated development team of 120+ C&R & 200+ CMC staff located in Shanghai, Suzhou & Florham Park, New Jersey



Broad bandwidth & capacity of R&D team enables smooth coordination of >25 trials globally & in China

Important working relationships with China & global regulators – potentially multiple new global registration studies in 2021

At launch / filing stage on 3 lead assets – major regulatory achievements



#### Fruquintinib (ELUNATE<sup>®</sup> in China)

- 1<sup>st</sup> China-discovered & developed, unconditionally approved cancer therapy
- Global Ph.III started mid-2020, >150 sites in U.S., E.U. & JP
- Ideal combo candidate with limited off-target activity; favorable PoC results with chemo & TKIs

#### Savolitinib

- 😋 China NDA 1<sup>st</sup> NDA approved globally and
  - first-in-class in China
- Global partnership with AZ China clinicals by HUTCHMED
- Multiple global indications potentially 5 reg. studies 2021

#### Surufatinib (SULANDA® in China)

- 🞯 2 China NDAs unpartnered
- U.S. NDA and E.U. MAA submission using China Ph.IIIs & U.S. Ph.Ib/II data
- Dual-MoA anti-angiogenesis and immuno-oncology

### 6 assets in global development

#### Rapid expansion of our U.S./E.U. clinical & regulatory team



HIGHLY DIFFERENTIATED NME PORTFOLIO AND GLOBAL PIPELINE

Program	Treatment	Indication	Target patient	Study name	Sites	Dose finding / safety run-in	Proof-of-concept	Registration
	Savolitinib + TAGRISSO®	NSCLC	2L/3L EGFRm; Tagrisso <sup>®</sup> ref.; MET+	SAVANNAH	Global	Oxnard/Ahn – DF/SMC		
	Savolitinib + IMFINZI® (PD-L1)	Papillary RCC	MET+	SAMETA	Global	In planning		
Savolitinib	Savolitinib + IMFINZI® (PD-L1)	Papillary RCC *	All	CALYPSO	UK/Spain	Powles – Queen Mary's		
MET	Savolitinib + IMFINZI® (PD-L1)	Clear cell RCC *	VEGFR TKI refractory	CALYPSO	UK/Spain	Powles – Queen Mary's		
	Savolitinib	Gastric cancer *	MET+	VIKTORY	S Korea	Lee – Samsung Med. Ctr		
	Savolitinib	Colorectal cancer *	MET+		US	Strickler – Duke Uni		
	Surufatinib	NET	Refractory		US	Dasari/Yao – MD Anderson		
Surufatinib	Surufatinib	NET	Refractory		EU	Garcia-Carbonero – UCM		
VEGFR 1/2/3;	Surufatinib	Biliary tract cancer			US	Li – City of Hope		
FGFR1; CSF-1R	Surufatinib	Soft tissue sarcoma			US	Patel/Tapp - MD And/ MSKCC		
	<b>Suru.</b> + tislelizumab (PD-1)	Solid tumors			US/EU			
	Fruquintinib	Colorectal cancer	Refractory	FRESCO-2	US/EU/JP	Eng/Desari – MD And. [1]		
Fruquintinib	Fruquintinib	Breast cancer			US	Tripathy - MD And.		
VEGFR 1/2/3	Fruq. + tislelizumab (PD-1)	TN breast cancer			US	In planning - IND cleared		
	Fruq. + tislelizumab (PD-1)	Solid tumors			TBD	In planning - IND cleared		
HMPL-689	HMPL-689	Healthy volunteers			Australia			
ΡΙ3Κδ	HMPL-689	Indolent NHL			US/EU	Zinzani – U of Bologna		
HMPL-523	HMPL-523	Indolent NHL			Australia			
Syk	HMPL-523	Indolent NHL			US/EU	Strati/Abrisqueta – MD And. / Valld	'Hebron	
HMPL-306	HMPL-306	Solid tumors			US/EU			
IDH 1/2	HMPL-306	Hem. malignancies			US/EU			
HMPL-760	HMPL-760	Hem. malignancies			US/EU	In planning - IND cleared		
BTK, 3G		Ũ						

[1] in U.S., in E.U. Tabernero - Vall d'Hebron & Sobrero - Genova; \* Investigator initiated trials (IITs).

Note: MET = mesenchymal epithelial transition receptor; VEGFR = vascular endothelial growth factor receptor; EGFRm = epidermal growth factor receptor mutation; FGFR1 = fibroblast growth factor receptor 1; CSF-1R = colony stimulating factor-1 receptor; Syk = spleen tyrosine kinase; PI3Kδ = Phosphatidylinositol-3-Kinase delta; IDH = isocitrate dehydrogenase; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; NET = neuroendocrine tumors; NHL = Non-Hodgkin's Lymphoma.

### 9 assets in China development

#### ...8-10 registration studies planned to start in 2021



HUTCHMED

HIGHLY DIFFERENTIATED NME PORTFOLIO AND GLOBAL PIPELINE

Program	Treatment	Indication	Target patient	Study name	Sites	Dose find / safety run-in	Proof-of-concept	Registration
	Savolitinib	NSCLC	MET Exon 14 skipping		China	Lu Shun – SH Chest Hosp.		
Savolitinib	Savolitinib + TAGRISSO®	NSCLC	2L EGFR TKI ref. NSCLC; MET+	SACHI	China	In planning		
MET	Savolitinib + TAGRISSO®	NSCLC	Naïve MET+ & EGFRm NSCLC	SANOVO	China	In planning		
	Savolitinib	Gastric cancer	2L; MET+		China	Shen Lin - Beijing Cancer Hosp.		
	Surufatinib	Pancreatic NET	All	SANET-p	China	Xu Jianming – #5 Med. Ctr.		
	Surufatinib	Non-Pancreatic NET	All	SANET-ep	China	Xu Jianming – #5 Med. Ctr.		
Surufatinib	Surufatinib	Biliary tract cancer	2L; chemotherapy refractory		China	Xu Jianming – #5 Med. Ctr.		
VEGFR 1/2/3;	Suru. + TUOYI® (PD-1)	NEN, ESCC, BTC			China	Shen Lin – BJ Univ. Tmr.		
FGFR1; CSF-1R	Suru. + TUOYI® (PD-1)	SCLC, GC, Sarcoma			China	Shen Lin – BJ Univ. Tmr.		
	Suru. + TUOYI® (PD-1)	TC, EMC, NSCLC			China	Shen Lin – BJ Univ. Tmr.		
	Suru. + TYVYT® (PD-1)	Solid tumors			China			
	Fruquintinib	Colorectal cancer	≥3L; chemotherapy refractory	FRESCO	China	Li Jin - Fudan Univ.		
	Fruq. + TAXOL®	Gastric cancer	2L	FRUTIGA	China	Xu Ruihua – Sun Yat Sen		
Fruquintinib	Fruq. + TYVYT <sup>®</sup> (PD-1)	CRC, EMC, RCC, HCC			China	Guanghai Dai - PLA Gen. (CRC)		
VEGFR 1/2/3	Fruq. + TYVYT <sup>®</sup> (PD-1)	GI tumors			China	Jin Li – SH East Hosp. (Others)		
	Fruq. + geptanolimab (PD-1)	CRC			China	Yuxian Bai - Harbin Med. Uni.		
	Fruq. + geptanolimab (PD-1)	NSCLC			China	Shun Lu – SH Chest Hosp.		
	HMPL-689	FL, MZL			China	Cao/Zhou – Fudan/ Tongji		
HMPL-689	HMPL-689	MCL, DLBCL			China	Cao/Zhou – Fudan/ Tongji		
ΡΙ3Κδ	HMPL-689	CLL/SLL, HL			China	Cao/Zhou – Fudan/ Tongji		
HMPL-523	HMPL-523	B-cell malignancies	All		China	Multiple leads by sub-types		
Syk	HMPL-523	ITP	All		China	Yang – CN Hem. Hosp.		
HMPL-453 FGFR 1/2/3	HMPL-453	IHCC			China	Jianming Xu - BJ 307 Hosp.		
HMPL-306	HMPL-306 (IDH1/2)	Hem. malignancies			China			
HMPL-295	HMPL-295 (ERK, MAPK pathway)	Solid tumors			China			
Epitinib	Epitinib (EGFR)	Glioblastoma	EGFR gene amplified		China	Ying Mao - SH Huashan		

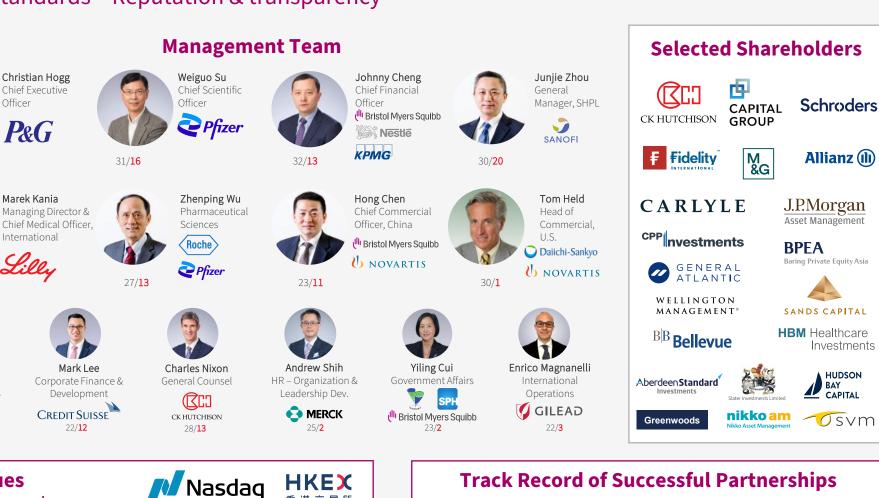
Note: NSCLC = Non small cell lung cancer; NENs = Neuroendocrine neoplasms; ESCC = Esophageal squamous-cell carcinomas; BTC = Biliary tract cancer; SCLC = Small cell lung cancer; GC = Gastric cancer; TC = Thyroid cancer; EMC = Endometrial cancer; CRC = Colorectal cancer; RCC = Renal cell cancer; HCC = Hepatocellular carcinoma; GI = Gastrointestinal; FL = Follicular lymphoma; MZL = Marginal zone lymphoma; MCL = Mantle cell lymphoma; DLBCL = Diffuse large B cell lymphoma; CLL/SLL = Chronic lymphocytic leukemia/Small lymphocytic lymphoma; HL = Hodgkin's lymphoma; ITP = immune thrombocytopenic purpura; IHCC = Intrahepatic cholangiocarcinoma.

### Seasoned executives – MNC veterans

London

Stock Exchange

#### Global standards – Reputation & transparency



AstraZeneca

Across functions verified by our long-term MNC partners

xx/xx Years in industry/at HUTCHMED; Company logos denote prior experience.

**SEASONED MGMT TEAM & STRONG** GOVERNANCE



32/21



Officer

27/3



May Wang Business Dev. & Strategic Alliances



0 Issues

in governance in

5 years on NASDAQ

15 years listed on AIM &

CREDIT SUISSE



Investments



AGRCK







### REALIZING GLOBAL POTENTIAL OF NOVEL ONCOLOGY ASSETS

# Attack cancer from multiple angles at same time



Need combinations of potent, yet tolerable drugs against specific targets

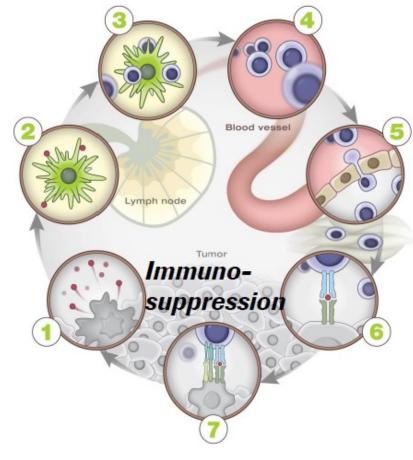
### Immune Desert

#### Insufficient T cell response

- Chemotherapies
- Vaccines
- CAR-T (pro-inflammatory strategies)
- TCB's

### Antigen Release Aberrant genetic drivers

• Targeted therapies (small molecule & antibody)



### Excluded Infiltrate

Inadequate T cell homing

- Anti-angiogenics
- Stromal targets
- Chemokines
- Vaccines

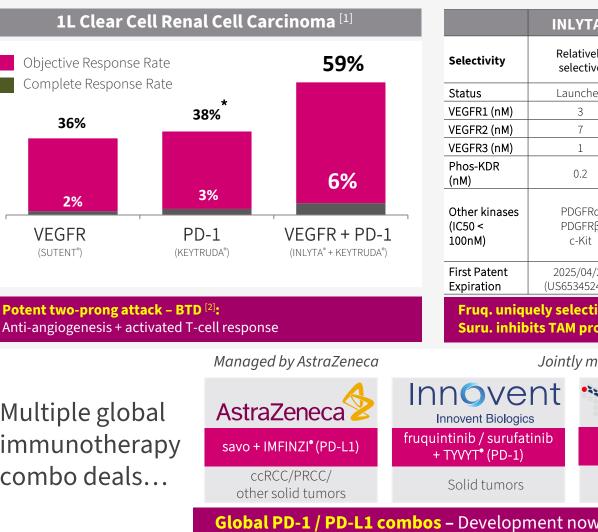
### **Inflamed** Inactivated T cell response

- Immunotherapies (address negative regulators)
- Vaccines

### **Immunotherapy combinations**



#### assets potentially ideal TKI combo partners for immunotherapy



	INLYTA®	LENVIMA®	Fruquintinib	Surufatinib
Selectivity	Relatively selective	Relatively selective	Highly selective	Selective angio- immuno kinase inhibitor
Status	Launched	Launched	Launched	Launched
VEGFR1 (nM)	3	22	33	2
VEGFR2 (nM)	7	4	25	24
VEGFR3 (nM)	1	5	0.5	1
Phos-KDR (nM)	0.2	0.8	0.6	2
Other kinases (IC50 < 100nM)	PDGFRα PDGFRβ c-Kit	PDGFRα PDGFRβ FGFR1-4 Ret c-Kit	none	<b>CSF-1R</b> FGFR1 FLT3 TrkB
First Patent Expiration	2025/04/29 (US6534524B1)	2021/10/19 (US7253286B2)	2029 (without extension)	2030 (without extension)

**Frug. uniquely selective** – unlike other TKIs with off-target toxicity Suru. inhibits TAM production – amplifying PD-1 induced immune response

Jointly managed by HUTCHMED & partners

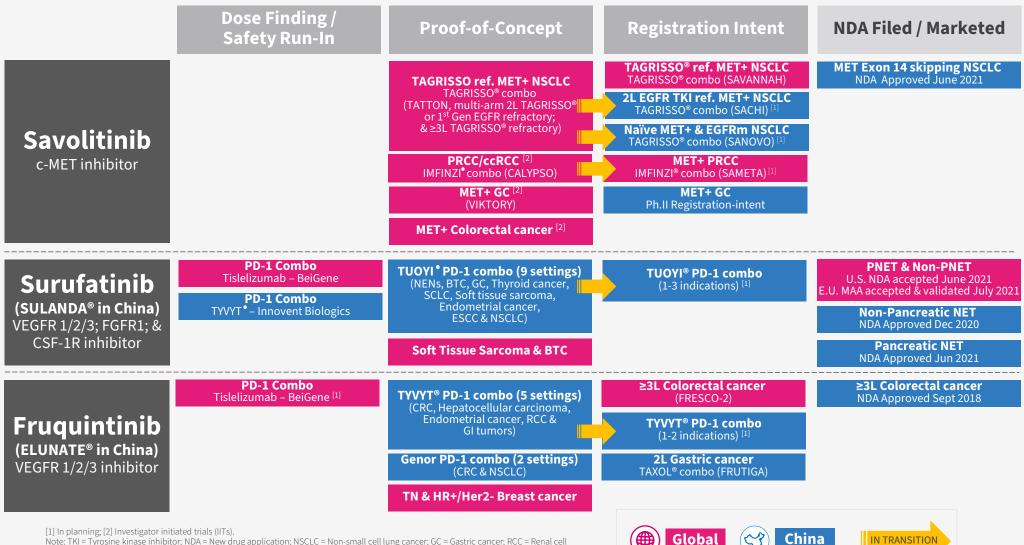


[1] Sources: (i) B. Rini et al for the for the KEYNOTE-426 Investigators, NEJM 2019 Feb 16. doi: 10.1056/NEJMoa1816714, Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma; (ii) D.F. McDermott et al, ASCO 2018 #4500, Pembrolizumab monotherapy as first-line therapy in advanced clear cell renal cell carcinoma (accRCC): Results from cohort A of KEYNOTE-427; \* ORR=38.2% for all PD-L1 expression combined positive scores (CPS) – ORR=50.0% for CPS≥1 pts, ORR=26.4% for CPS<1 pts.; [2] BTD = Breakthrough Therapy Designation.

### Maximizing the value of our lead assets



#### 3 marketed products, 1 NDA under review & 8-10 reg. studies by mid-2021



Note: TKI = Tyrosine kinase inhibitor; NDA = New drug application; NSCLC = Non-small cell lung cancer; GC = Gastric cancer; RCC = Renal cell carcinoma; NET = Neuroendocrine tumor; BTC = Biliary tract cancer; ESCC = Esophageal squamous cell carcinoma; SCLC = Small cell lung cancer; CRC = Colorectal cancer; GI = Gastrointestinal; TN = Triple negative.

### **Deep NME early pipeline**



#### Multiple further waves of innovation progressing

	IND preparation	Dose Finding/ Safety Run-In	Proof-of Concept	<b>Registration Intent</b>
HMPL-689 PI3Kδ inhibitor		<b>inhl</b> (CBCL, CLL, FL, MCL, MZL, PTCL, WM/LPL)	<b>6 iNHL settings</b> (FL, MZL, MCL, DLBCL, CLL/SLL, HL)	<b>iNHL</b> – Ph.II Registration-intent (FL, MZL; other iNHL planned)
HMPL-523 Syk inhibitor		<b>inhl</b> (CBCL, CLL, FL, MCL, MZL, PTCL, WM/LPL)	<b>6 iNHL settings</b> (CLL/SLL, aggressive NHL, MCL, FL, MZL, WM)	
HMPL-453 FGFR 1/2/3/ inhibitor			ІТР	ITP – Ph.III <sup>[1]</sup>
HMPL-306 IDH1/2 inhibitor		2x Hematology & Solid Tumors AML		
HMPL-295 ERK inhibitor		Solid tumors		
Oncology discovery		<i>hina INDs submitted; 2 new co</i> L-653 (solid tumors) and HMPL-A83		<b>U</b>
Immunology discovery	4 new candidates in precl	linical-INMAGENE collabor	ration	

Note: iNHL = Indolent non-Hodgkin's lymphoma; CBCL = Cutaneous B-cell lymphoma; CLL/SLL = Chronic lymphocytic leukemia / Small lymphocytic lymphoma; FL = Follicular lymphoma; MCL = Mantle cell lymphoma; MZL = Marginal zone lymphoma; PTCL = Peripheral T-cell lymphoma; WM = Waldenström's macroglobulinemia; LPL = Lymphoplasmacytic lymphoma; DLBCL = Diffuse large B-cell lymphoma; ITP = Immune Thrombocytopenic Purpura; IHCC= Intrahepatic Cholangiocarcinoma; AML = Acute Myeloid Leukemia.

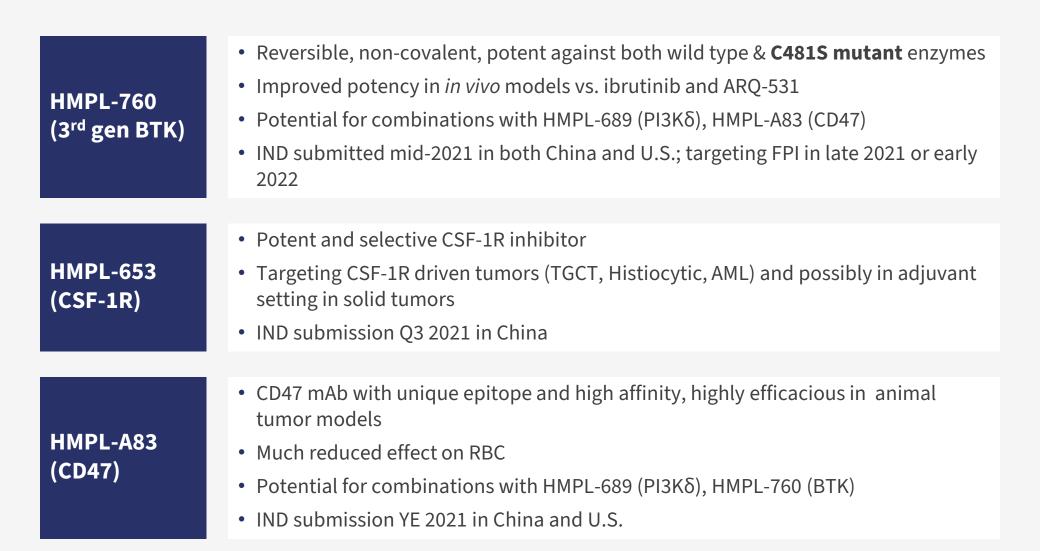


### Early programs summary



HMPL-453 (FGFR1/2/3)	<ul> <li>Phase II in iHCC with FGFR2 fusion enrolling</li> <li>Early signs of clinical activity</li> <li>Combinations study IND filed mid-2021: 1L chemo &amp; IO combos FPI in late 2021 or early 2022</li> </ul>	t tennegenergenergenergenergenergenergener
HMPL-306 (IDH1/2)	<ul> <li>Potent IDH1/2 inhibitor with brain penetration</li> <li>Designed to overcome resistance due to isoform conversion in MDS/AML, and explore GBM</li> <li>Dose escalation in China and the U.S. ongoing, targeting completion in late 2021 or early 2022</li> </ul>	Autor of Autor Autor of Autor Autor Autor of Autor
HMPL-295 (ERK)	<ul> <li>First candidate in MAPK pathway, more to come from HUTCHMED</li> <li>Dose escalation enrolling in China</li> </ul>	RAS NET

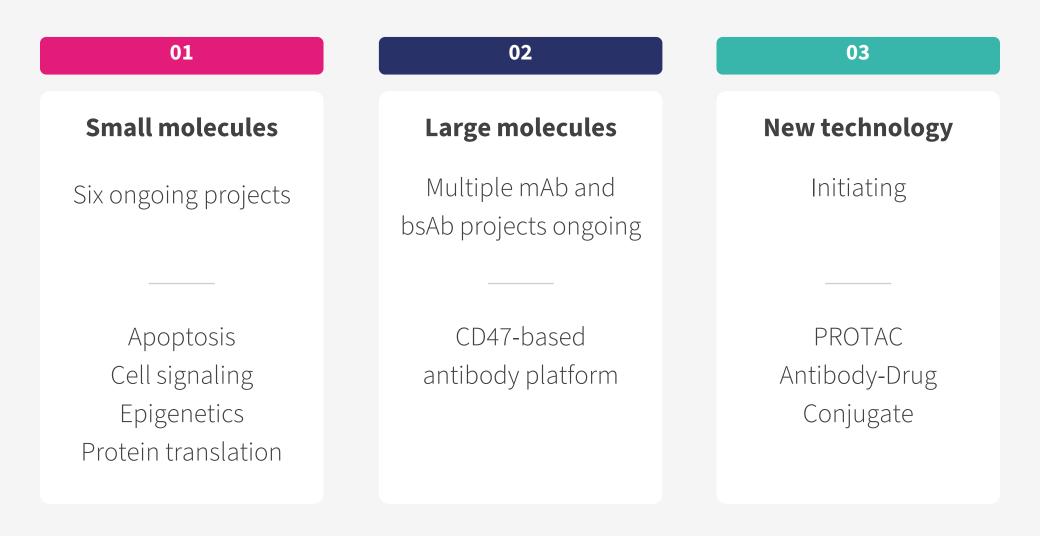
### New candidates' INDs submitted/planned for '21



HUTCHM

### **Discovery Project Overview**









### BUILDING A FULLY INTEGRATED ONCOLOGY BUSINESS IN CHINA & U.S.

### China and U.S. are key oncology markets



#### CHINA

#### ~25% of world cancer patients <sup>[1]</sup>

#### Industry's attention turning to unmet medical need in China oncology

- Regulatory reforms in China addressing low SoC<sup>[2]</sup>
- Major investment inflow

#### **HUTCHMED** is a first mover

- ELUNATE<sup>®</sup> launch in 3L mCRC; First ever in China<sup>[3]</sup>
- Deep pipeline 11 clinical drug candidates with 3 NDAs submitted in China

#### Major commercial opportunity

National Drug Reimbursement; Medical coverage

#### **U.S.**

#### ~40% of global oncology medicine spending <sup>[4] [5]</sup>

#### Innovation is being rewarded

- Oncology medicine spending grew to \$72 billion in 2020 from \$45 billion in 2016, driven primarily by proprietary brands
- Oncology medicine spending is expected to exceed \$110 billion by 2025, even after considering savings from biosimilar introduction
- Regulators continue to utilize programs for expedited development of medicines for serious conditions

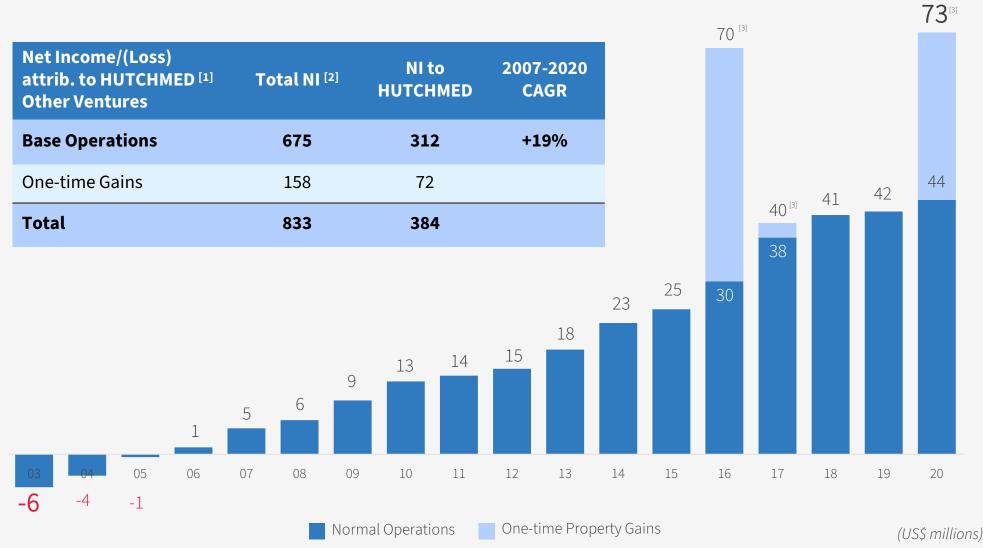
### Positioned to complement high usage of PD-1/L1 inhibitors

- HUTCHMED's portfolio of TKIs, designed for clinical differentiation, are being studied in combination with PD-1/L1 inhibitors in China
- Global studies initiated or in planning for all three late-stage assets

### HUTCHMED competence in China operations

HUTCHMED

#### A 17-year track record of 19% CAGR net income growth in our Other Ventures businesses

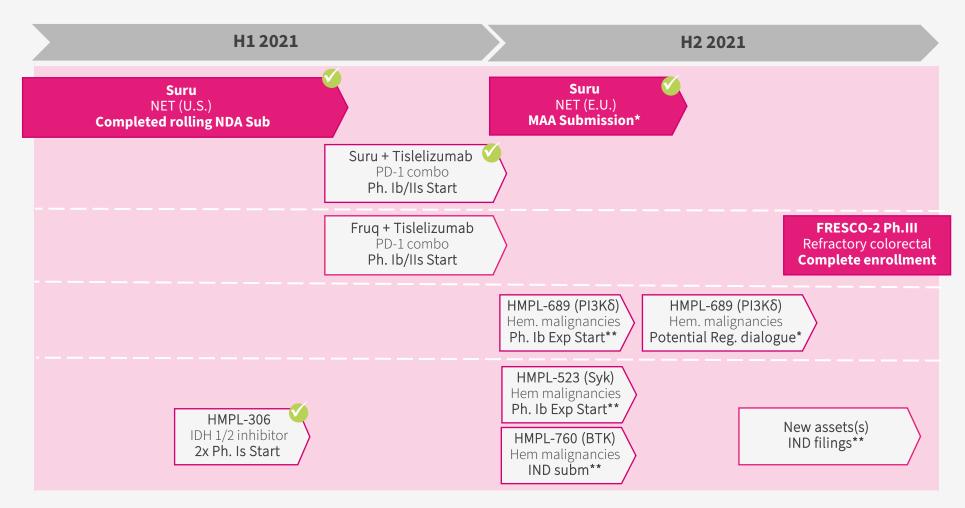


[1] 2003–2006 incl. disco. operation; [2] Based on aggregate Non-GAAP net income / (loss) of consolidated subsidiaries and non-consolidated joint ventures of Other Ventures, please see appendix "Non-GAAP Financial Measures and Reconciliation"; [3] Includes the land compensation in SHPL of \$40.4 million from net income attributable to HUTCHMED in 2016, SHPL's R&D related subsidies of \$2.5 million from net income attributable to HUTCHMED in 2017 and the land compensation in HBYS of \$28.8 million from net income attributable to HUTCHMED in 2020.

### **International development**



Rapid expansion of our U.S./E.U. clinical & regulatory team, progressing a broad clinical portfolio of trials and regulatory engagements



Note: excludes savolitinib which is being developed globally by AstraZeneca

\* subject to regulatory interaction; \*\* subject to supportive data.



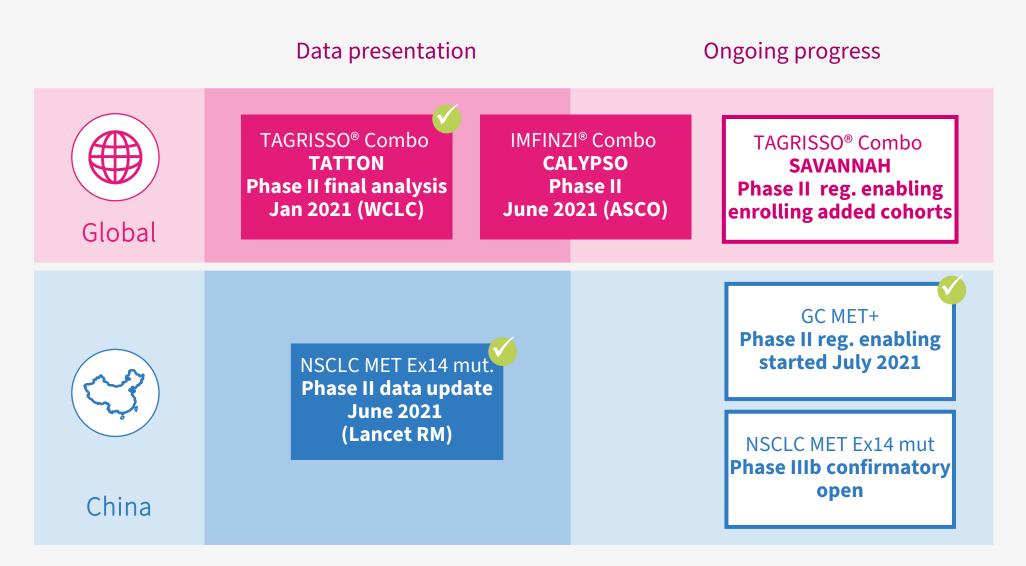
# A3a

### SAVOLITINIB

A highly selective small molecule inhibitor of MET being developed broadly across MET-driven patient populations in lung cancer, gastric cancer and renal cell carcinoma

### Savolitinib clinical development updates

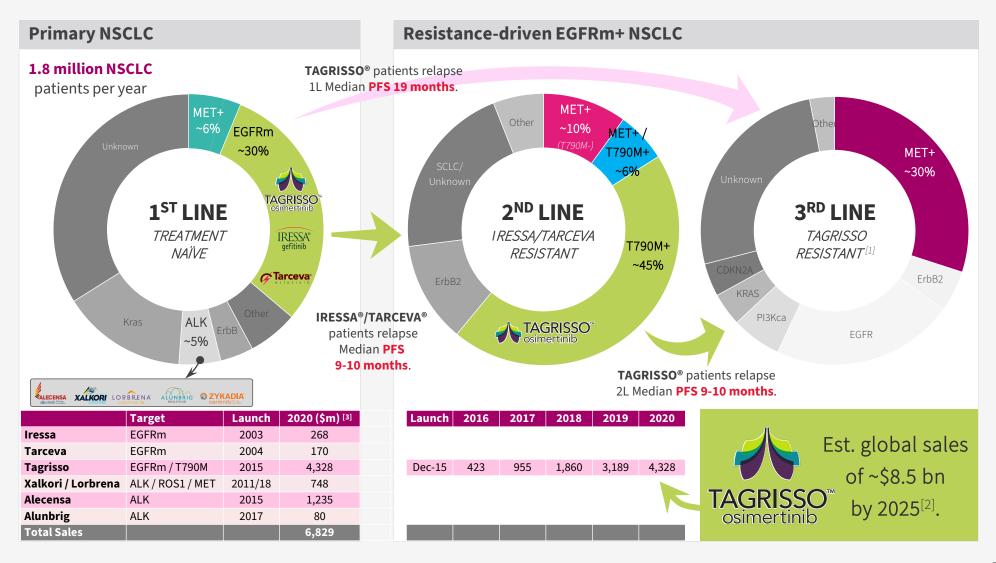




### **NSCLC by driver aberration**



#### Biggest opportunity is MET+ (mutant / gene amplified) NSCLC



[1] Primary drivers, based on aggregate rociletinib/TAGRISSO® data published at 2016/2017 ASCO; [2] Research estimates & including adjuvant approval; [3] company annual reports and Frost & Sullivan.

# Savolitinib: MET Exon14 skipping alterations

### NDA approved June 2021 in China

### NSCLC with MET Exon14 skipping alterations

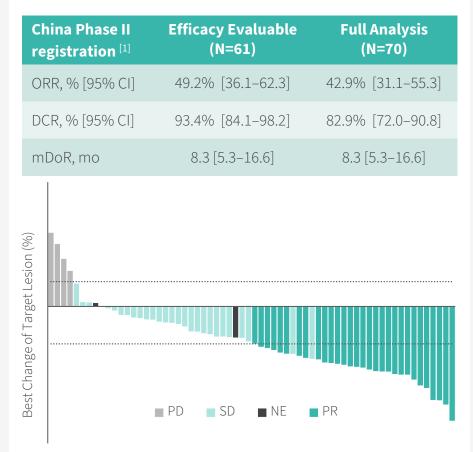
- 2-3% of NSCLC, up to 22% in PSC
- Most common in elderly patients
- No effective treatments with poor prognosis

# MET Exon14 skipping alterations in other tumor types

- Secondary GBM
- GI tumors
- Histiocytic sarcoma

## Phase II in NSCLC harboring MET Exon 14 skipping alterations (data by IRC)

HUTCHM



[1] Independent Review Committee assessed analysis. Investigator-assessed evaluable ORR=53.2%, DCR=91.9%.

Lu S, Fang J, Li X, et al. Once-daily savolitinib in Chinese patients with pulmonary sarcomatoid carcinomas and other non-small-cell lung cancers harbouring MET exon 14 skipping alterations: a multicentre, single-arm, open-label, phase 2 study. Lancet Respir Med. Published online June 21, 2021. https://doi.org/10.1016/S2213-2600(21)00084-9

# Savolitinib – MET Exon 14 skipping NSCLC



### China's lead selective MET inhibitor

### Competitive landscape outside China:

Treatment Line	MET aberration	N	BICR <sup>[1]</sup> ORR (%)	DCR (%)	mDoR (months)	mPFS (months)
Capmatinib <sup>[2][3]</sup>						
1L (cohort 5b)	Ex14 skipping	28	<b>68</b> [48, 84]	<b>96</b> [82, 100]	12.6 [5.6, NE]	<b>12.4</b> [8.2, 23.4]
2/3L (cohort 4)	Ex14 skipping	69	<b>41</b> [29, 53]	<b>78</b> [67, 87]	<b>9.7</b> [5.6, 13.0]	<b>5.4</b> [4.2, 7.0]
2L (cohort 6, group 2)	Ex14 skipping	31	<b>52</b> [33, 70]	<b>90</b> [74, 98]	8.4 [4.2, NE]	<b>6.9</b> [4.2, 13.3]
1L (cohort 7)	Ex14 skipping	32	<b>66</b> [47, 81]	<b>100</b> [89, 100]	NE	10.8 [6.9, NE]
1L (cohort 5a)	Amp (GCN≥10)	15 [4]	<b>40</b> [16, 68]	<b>67</b> [38, 88]	<b>7.5</b> [2.6, 14.3]	<b>4.2</b> [1.4, 6.9]
2/3L (cohort 1a)	Amp (GCN ≥10)	69	<b>29</b> [19, 41]	<b>71</b> [59, 81]	<b>8.3</b> [4.2, 15.4]	<b>4.1</b> [2.9, 4.8]
Tepotinib						
44% 1L/ 56% ≥2L <sup>[5]</sup>	Ex14 skipping	99 [6]	<b>46.5</b> [36.4,56.8]	<b>65.7</b> [55.4, 74.9]	<b>11.1</b> [7.2, NE]	<b>8.5</b> [6.7, 11.0]
1-3L <sup>[7]</sup>	Amp	24	<b>41.7</b> [22.1-63.4]	45.9	<b>NE</b> [2.8, NE]	<b>4.2</b> [1.4, NE]

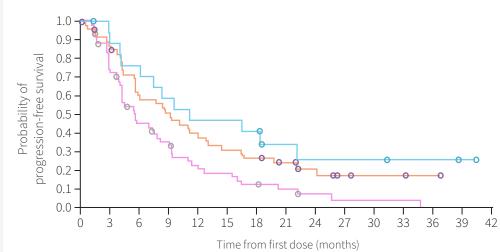
[1] BICR = blinded independent central review; [2] Wolf et al. "Capmatinib in MET Exon 14–Mutated or MET-Amplified Non–Small-Cell Lung Cancer." N Engl J Med 2020; 383:944-957 DOI: 10.1056/NEJMoa2002787; [3] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr 9020); [4] closed early due to slow enrollment; [5] Paik et al. "Tepotinib in Non–Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations." N Engl J Med 2020; 383:931-943 DOI: 10.1056/NEJMoa2004407; [6] patients followed for over 9 months; [7] ASCO 2021 J Clin Oncol 39, 2021 (suppl 15; abstr 9021).

## TATTON B & D data – PFS



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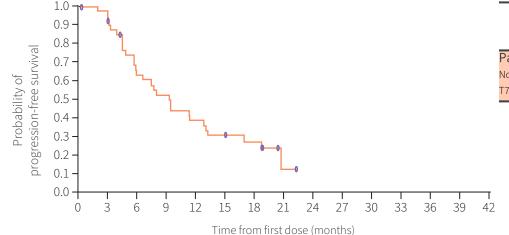
### TAGRISSO<sup>®</sup> + savolitinib in EGFR TKI refractory NSCLC

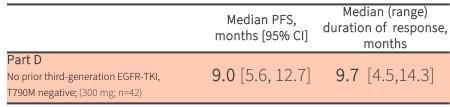


	Median PFS, months [95% CI]	Median (range) duration of response, months
Part B1 Prior third-generation EGFR-TKI; (600 mg <sup>[1]</sup> ; n=69)	5.5 [4.1, 7.7]	<b>9.5</b> [4.2, 14.7]
Part B2 No prior third-generation EGFR-TKI, T790M negative; (600 mg <sup>[1]</sup> ; n=51)	<b>9.1</b> [5.5, 12.8]	<b>10.7</b> [6.1, 14.8]
<b>Part B3</b> No prior third-generation EGFR-TKI, T790M positive; (600 mg <sup>[1]</sup> ; n=18)	<b>11.1</b> [4.1, 22.1]	<b>11.0</b> [2.8, NR]

#### Data-cut off date: March 4, 2020

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.





#### Data-cut off date: March 4, 2020

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.

PFS= Progression Free Survival; EGFR = Epidermal Growth Factor Receptor; TKI = Tyrosine Kinase Inhibitor; [1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed ≤55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily. Han JY, et al. Osimertinib + savolitinib in patients with EGFRm MET-amplified/overexpressed NSCLC: Phase Ib TATTON Parts B and D final analysis. WCLC January 2021 #FP14.03.





### TATTON B & D data – AEs & tolerability

Event, n (%)	All Part B (n=138) osimertinib 80 mg + savolitinib 600 mg [1]	Part D (n=42) osimertinib 80 mg + savolitinib 300 mg <sup>[1]</sup>
Any AE	138 (100)	41 (98)
Any AE possibly related to savolitinib	124 (90)	32 (76)
AE grade ≥3	86 (62)	21 (50)
AE possibly causally related to study treatment leading to discontinuation of:		
Savolitinib	49 (36)	15 (36)
Osimertinib	24 (17)	8 (19)
Any AE leading to death	7 (5)	2 (5)
Any SAE	67 (49)	16 (38)

[1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed <55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily. Part D data are preliminary, therefore, for osimertinib, the mean actual treatment exposure was 8.5 months vs 6.1 months for Parts B and D, respectively, and 7.1 months vs 4.9 months for savolitinib, for Parts B and D, respectively; Han JY, et al. Osimertinib + savolitinib in patients with EGFRm MET-amplified/overexpressed NSCLC: Phase Ib TATTON Parts B and D, respectively.

## TATTON B & D data – AEs & SAEs



### Most common AEs<sup>[1]</sup> independent of causality & SAEs (≥3%)<sup>[2]</sup>

	All Part B (n=138)		Part D	(n=42)	AE*, n (%)	All Part B (n=138)		Part D (n=42)	
AE*, n (%)	All	Grade	All	Grade	AL , II (70)	All grades	Grade≥3	All grades	Grade≥3
	grades	≥3	grades	≥3	Rash	26 (19%)	3 (2%)	8 (19%)	0
Nausea	67 (49%)	4 (3%)	13 (31%)	0	Stomatitis	26 (19)	0	4 (10)	0
Fatigue	48 (35)	6 (4)	4 (10)	0	Constipation	26 (19)	0	3 (7)	0
Decreased appetite	47 (34)	5 (4)	6 (14)	1 (2)	Pruritus	24 (17)	1(1)	5 (12)	0
Vomiting	46 (33)	6 (4)	5 (12)	0	Headache	23 (17)	0	3 (7)	0
Oedema peripheral	44 (32)	3 (2)	8 (19)	0	Myalgia	22 (16)	3 (2)	6 (14)	1 (2)
Diarrhoea	39 (28)	4 (3)	8 (19)	2 (5)	Cough	22 (16)	0	4 (10)	1 (2)
Paronychia	30 (22)	3 (2)	7 (17)	0	AST increased	21 (15)	9 (7)	2 (5)	0
Pyrexia	29 (21)	1(1)	6 (14)	0	Pneumonia	15 (11)	7 (5)	7 (17)	5 (12)

SAE**, n (%)	All Part B (n=138)	Part D (n=42)
Pneumonia	7 (5%)	4 (10%)
Anaphylactic reaction	6 (4)	1 (2)
Pneumothorax	6 (4)	1 (2)
Pyrexia <sup>#</sup>	5 (4)	0
Dyspnoea	5 (4)	0
Drug hypersensitivity	4 (3)	1 (2)
Diarrhoea	4 (3)	1 (2)
Back pain	4 (3)	0

[1] ≥15% in either Part B or Part D for all grades; [2] ≥3% in either Part B or Part D for all grades. <sup>#</sup>The emergence of drug-related hypersensitivity AEs are characterised by events such as pyrexia; The emergence of hypersensitivity and anaphylaxis events led to a protocol amendment introducing a weight-based savolitinib dosing regimen (for the last group of patients enrolled in Part B) in parallel to the lower dose of savolitinib (300 mg) being tested (for all patients enrolled in Part D)

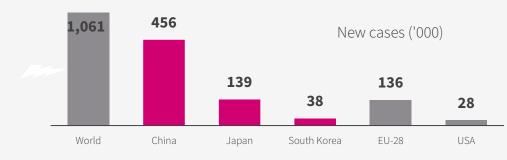
Sequist LV, Han JY, Ahn MJ, et al. Osimertinib plus savolitinib in patients with EGFR mutation-positive, MET-amplified, non-small-cell lung cancer after progression on EGFR tyrosine kinase inhibitors: interim results from a multicentre, open-label, phase 1b study. Lancet Oncol. 2020; S1470-2045(19)30785-5. doi:10.1016/S1470-2045(19)30785-5

# Savolitinib – MET+ gastric cancer



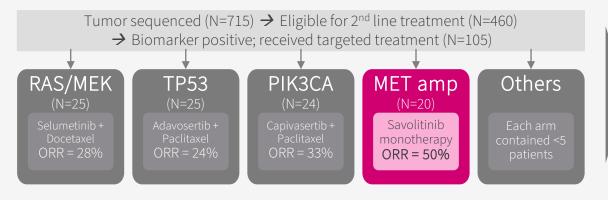
A major problem in east Asia – Japan, Korea & China

### 1. Gastric (stomach) cancer is the 4<sup>th</sup> most common cancer globally – 768,000 deaths/year

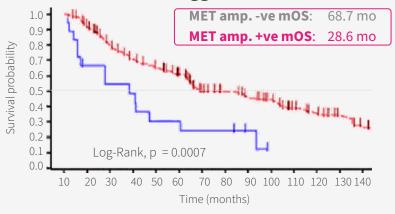


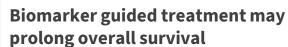
World Cancer Research Fund International, WHO, ACS, NCCR, Lancet, Frost & Sullivan Analysis.

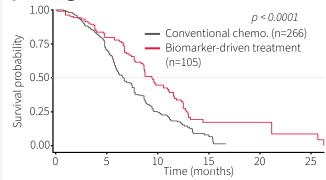
### 3. VIKTORY: Highest response rate in savolitinib monotherapy arm<sup>[2]</sup>



#### 2. MET+ disease is more aggressive <sup>[1]</sup>



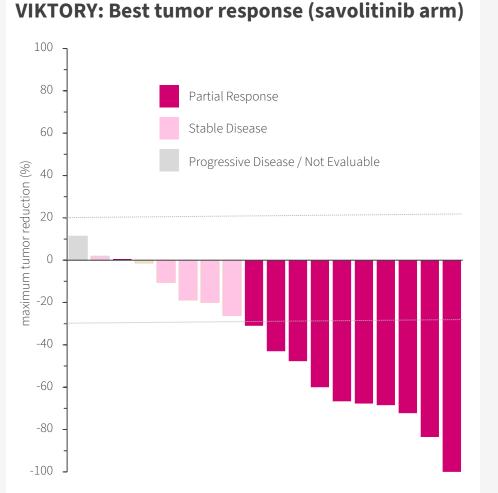




Catenacci DV, Ang A, Liao WL, et al. MET tyrosine kinase receptor expression and amplification as prognostic biomarkers of survival in gastroesophageal adenocarcinoma. Cancer. 2017;123(6):1061-1070. doi:10.1002/cncr.30437.
 Lee, et al. "Tumor genomic profiling guides metastatic gastric cancer patients to targeted treatment: The VIKTORY Umbrella Trial." Cancer Discov. 2019 Jul 17. pii: CD-19-0442. doi: 10.1158/2159-8290.CD-19-0442.

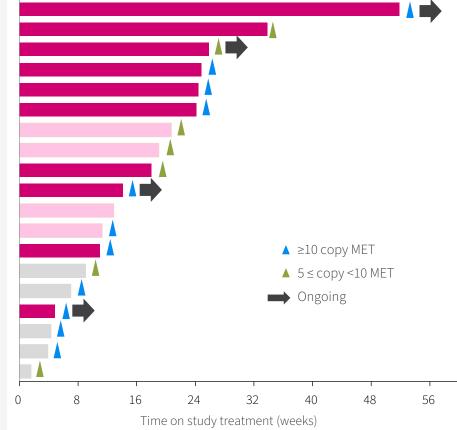
# Savolitinib recap: MET ampl. in gastric cancer

Phase II trial ongoing in China with potential for registration





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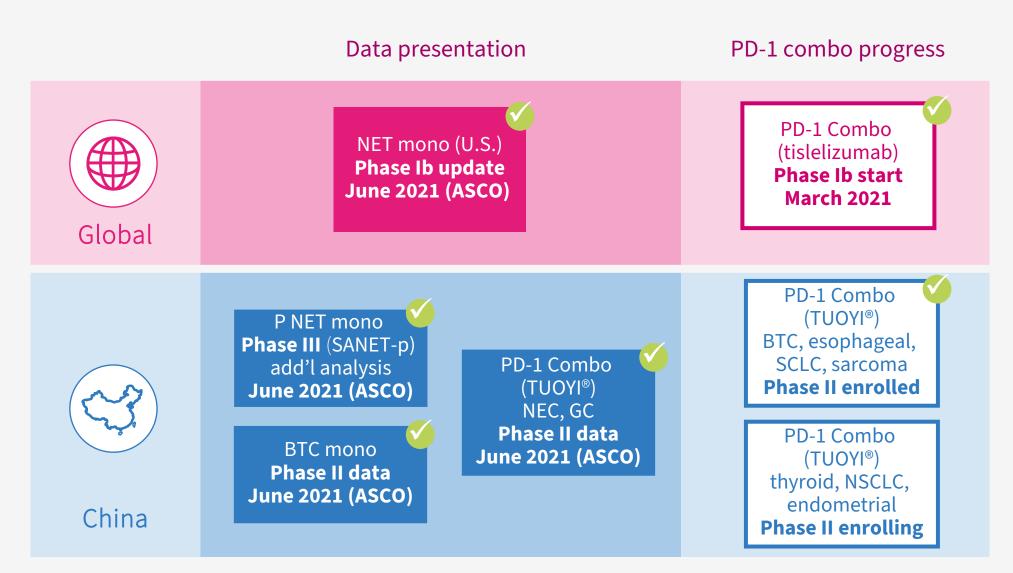


# A3b

SURUFATINIB (SULANDA<sup>®</sup> IN CHINA)

A small molecule inhibitor of VEGFR, FGFR & CSF-1R designed to inhibit tumor angiogenesis and promote the body's immune response against tumor cells via tumor associated macrophage regulation

## Surufatinib clinical development updates



litette

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## Surufatinib

## Overview of NET – 140,000~170,000 patients in the U.S. [1][2][3]

### What are neuroendocrine tumors ("NET")?

- ~2% of all malignancies
- Tumor begins in the specialized cells of the body's neuroendocrine system. Cells have traits of both hormone-producing endocrine cells & nerve cells
- Found throughout the body's organs. Most NETs take years to develop but some can grow fast

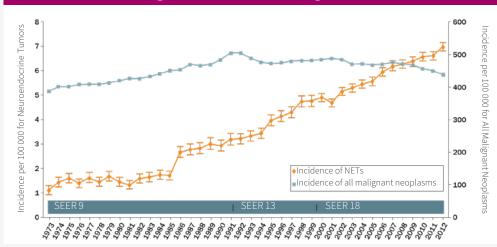
### Hormone-related symptoms <sup>[1]</sup>

 Functional NETs (~8-35% of patients) release hormones / peptides causing symptoms like diarrhea & flushing; Non-functional NETs have no symptoms

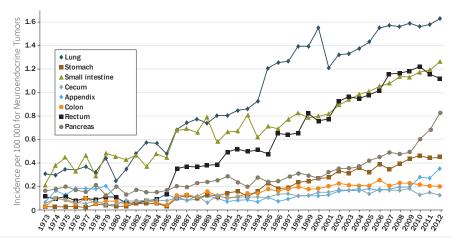
### Differentiation & biomarkers for grading:

- Well differentiated: look like healthy cells grow slowly; Poorly differentiated: look less like healthy cells – grow quickly;
- Mitotic count Mitosis is process by which tumor cells grow & divide; Ki-67 index Ki-67 a protein that increases as cells divide.

NET growth – better diagnosis<sup>[4]</sup>



NET epidemiology – highly fragmented<sup>[4]</sup>

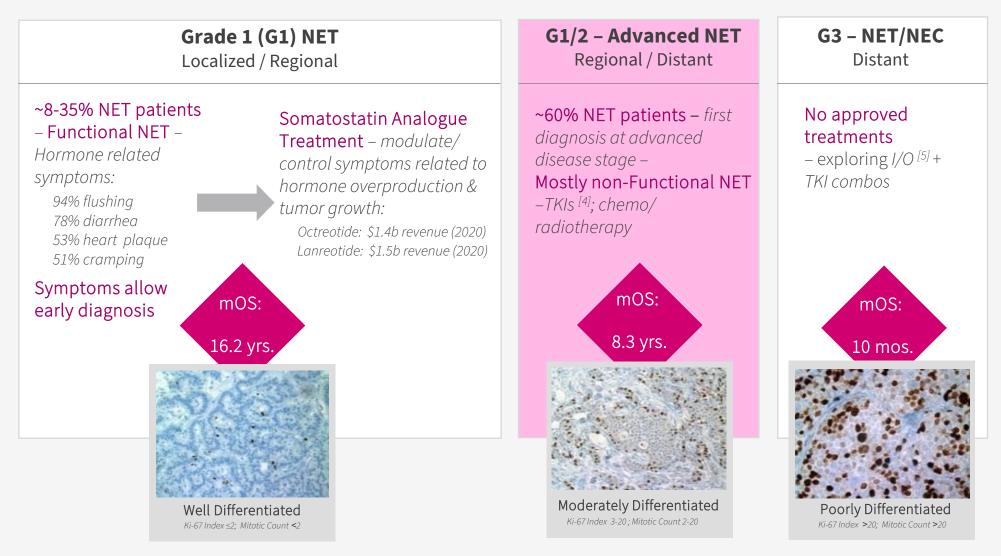


[1] Frost & Sullivan; [2] www.cancer.net (patient information from ASCO) – NET is a subtype of neuroendcrine neoplasms, NENs); [3] IQVIA 2019; [4] Dasari A, et al.: Trends in the Incidence, Prevalence, & Survival Outcomes in Patients With Neuroendocrine Tumors in the U.S.. JAMA Oncol. 2017;3(10):1335–1342.

# High-level NET landscape



### Long-term disease – rapid deterioration in later stages <sup>[1][2][3]</sup>



[1] Arvind Desari et. al. Trends in the Incidence, Prevalence, and Survival Outcomes in Patients With Neuroendocrine Tumors in the U.S., JAMA Oncol. 2017;3(10):1335–1342; [2] Van Cutsem et al. ESMO – Neuroendocrine Tumors Diagnostic & Therapeutic Challenges; [3] mOS = median overall survival; [4] TKIs = Tyrosine Kinase Inhibitors; [5] I/O = Immuno oncology/immunotherapy

# G1/2 Advanced NET <sup>[1]</sup> (Ki-67 Index 0-20)

## Global opportunity in lung/other NETs & China wide-open

Octreotide Lanreotide <sup>177</sup>Lu-Dotatate Site est. % Streptozocin Sunitinib **Everolimus** Surufatinib LAR autogel Progressed in past Progressed in past Progressed in past **Disease status** Treatment naïve Stable disease Progressed in past 3 yrs. Historical 12 mo. 6 mo. 12 mo. CLARINET<sup>[2]</sup> RADIANT-4<sup>[3]</sup> Historical Ph. II Stomach 6% SANET-ep SSR over expression CLARINET<sup>[2]</sup> RADIANT-4<sup>[3]</sup> Small bowel / PROMID NETTER-1 SANET-ep 20% appendix **GI Tract** CLARINET<sup>[2]</sup> RADIANT-4<sup>[3]</sup> Historical Ph. II **Colon & Rectum** SANET-ep 20% SSR over expression CLARINET<sup>[2]</sup> Historical Ph. II RADIANT-3<sup>[3]</sup> PHASE III 6% SANET-p **Pancreas** Historical SSR over expression RADIANT-4<sup>[3]</sup> SANET-ep 27% Lung SANET-ep Other ~10% Other RADIANT-4<sup>[3]</sup> Unknown SANET-ep ~10% **Primary** 

[1] Yao ESMO 2019; [2] CLARINET approved only for Ki-67 Index <10 (i.e. est. ~50% of G1/G2); [3] Everolimus approved in non-Functional NET (~60% pNET; 90% Lung NET; majority mid-gut/small bowel NET).

# HUTCHMED

🛞 Global 🥎 China

## 140,000~170,000 NET patients in U.S. [1][2]



### U.S. NET treatment landscape – highly fragmented

		Somatostatin Based Therapi	es	Ki	nase Inhibitor Therapies	
	Sandostatin <sup>®</sup> LAR (octreotide)	Somatuline Depot <sup>®</sup> (lanreotide)	Lutathera° ( <sup>177</sup> Lu-Dotatate)	Afinitor <sup>®</sup> (everolimus)	Sutent <sup>®</sup> (sunitinib)	Surufatinib (Approved in China)
2020 Sales	\$1.4bn	\$1.5bn	\$0.4bn	\$1.1bn	\$0.8bn	-
MOA <sup>[3]</sup>	Somatostatin analogue	Somatostatin analogue	Somatostatin receptor targeting radiotherapy	mTOR inhibition	Inhibits multiple receptor tyrosine kinases	VEGFR/FGFR1 & CSF-1R inhibition
Admin.	Subcutaneous or intramuscular inj. (LAR)	Subcutaneous injection	Intravenous inj. (radio-qualified physicians).	Oral tablet	Oral capsules	Oral capsules
Shelf-life	3 years	2 years	72 hours	3 years	3 years	2+ years <sup>[5]</sup>
Dosage	2 wks: Sando. inj. 0.1-0.6mg per day; then 2 months Sando. LAR 20mg per 4 wks.	120mg inj. every 4 wks.	7.4GBq (one ~25ml vial) inj. every 8 wks – 4 doses total.	10mg orally once daily.	37.5mg taken orally once daily.	300mg orally once daily.
NET indication /s	diarrhea & flushing from meta. carcinoid tumors.	<ul> <li><u>GEP-NETs</u>: unresectable, well or moderately diff., (locally adv. or meta) GEP-NETs to improve PFS.</li> <li><u>Carcinoid Syndrome</u>: to reduce frequency of short-acting somatostatin rescue therapy.</li> </ul>	positive GEP-NETs.	<ul> <li><u>pNET</u>: progressive pNET (unresectable, locally adv. or meta).</li> <li><u>GI-NET or Lung NET</u>: progressive, well- diff., <i>non-functional</i> NET (unresectable, locally adv. or meta). Not for <i>functional</i> carcinoid tumors.<sup>[4]</sup></li> </ul>	differentiated pNET (unresectable locally adv. or meta).	<ul> <li>2 positive RCTs in <u>pNET</u> &amp; <u>epNET</u> in China</li> <li>epNET NDA approved in China; pNET under review</li> <li>U.S. NDA filing started YE20.</li> </ul>
Non-NET indication/s	Acromegaly; watery     diarrhea from VIPomas.	Acromegaly.		<ul> <li>Adv. HR+ HER2-n breast cancer; adv. 2L RCC; renal angiomyolipoma and TSC.</li> </ul>	<ul> <li>2L GIST; adv. RCC; high risk of recurrent RCC.</li> </ul>	

	Sandostatin° / Placebo	Somatuline Depot <sup>®</sup> / Placebo	Lutathera® + Sando. LAR / Sando. LAR		itor°/ cebo	Sutent° / Placebo		atinib / cebo
mPFS (mo.) primary EP	14.3/6.0	NR / 18.0	NR / 8.5	pNET 11.0 / 4.6	Lung & GI NET 11.0 / 3.9	pNET: 11.4 / 5.5	Ph III pNET 10.9 / 3.7	Ph III non-pNET 9.2 / 3.8
HR	0.34	0.47	0.21	0.35	0.48	0.42	0.49	0.33
( <i>p-value</i> )	0.000072	<0.001	<0.0001	<0.001	<0.001	<0.001	0.0011	<0.0001
ORR	2%/2%	NR	18%/3%	5%/2%	2%/1%	9% / 0%	19%/2%	10%/0%
DCR	69% / 40%	NR	95% / 76%	73%/51%	81%/64%	72% / 60%	81%/66%	87% / 66%
Pivotal	PROMID	CLARINET	NETTER-1	RADIANT-3	RADIANT-4	A6181111	SANET-p	SANET-ep

[1] Frost & Sullivan; [2] www.cancer.net (patient information from ASCO) – NET is a subtype of neuroendcrine neoplasms, NENs); [3] IQVIA 2019; [4] Dasari A, et al.: Trends in the Incidence, Prevalence, & Survival Outcomes in Patients With Neuroendocrine Tumors in the U.S.. JAMA Oncol. 2017;3(10):1335–1342.

# Surufatinib: U.S. NET Market Landscape

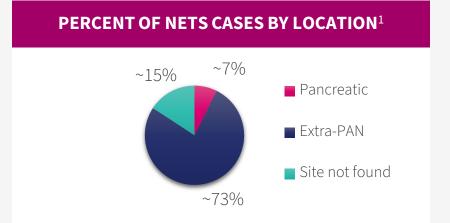


### A rare heterogeneous tumor that presents in the metastatic stage in 40-50% of patients

## NETs are relatively rare and heterogeneous tumor type, comprising ~2% of all malignancies<sup>1,2</sup>

### U.S. 2021 estimates: <sup>1,3</sup>

- 140,000~170,000 living with NET
  - 17,000~20,000 diagnosed with Extra-pancreatic NET
  - 1,200~3,900 diagnosed with pancreatic NET
- ~30,000 patients under active treatment in the metastatic setting
- 40%–50% of overall NET patients present with distant metastases at initial diagnosis<sup>6,7</sup>
  - Metastatic disease generally incurable and current treatments offer palliation only
- 5-year survival is 50~60% in Pancreatic NETs, 60~90% in GI-NETs and 60~90% in Lung NETs



#### **TREATMENT LANDSCAPE**

## Palliative systemic therapy is mainstay for adv. disease

- Somatostatin analogs
- Targeted Agents
  - Sunitinib
  - Everolimus
- Cytotoxics:
- Peptide receptor radionuclide therapy

## Surufatinib: U.S. extrapancreatic NET Prescriber Level Data



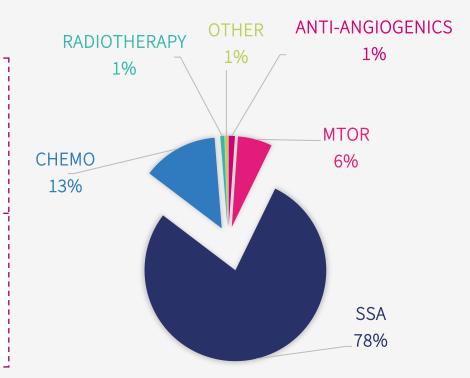
## < 10% of eligible patients are prescribed everolimus or sunitinib in 2018

# IQVIA's medical claims and prescription data longitudinal databases track patients over time and not dependent on insurance carrier, pharmacy, or employer.

- 1.0 billion annual claims that contain diagnosis and visit information
- Represents >870,000 practitioners per month.



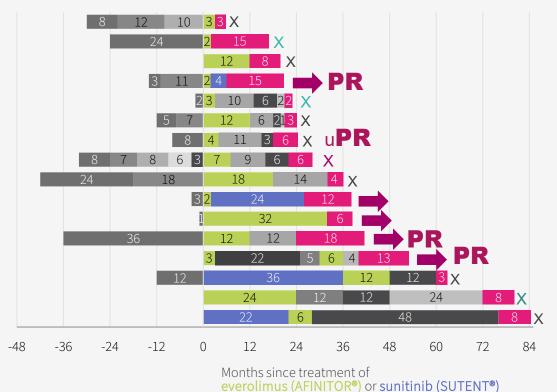
- Sourced from U.S. office-based physicians, and other private practitioners through the CMS-1500 medical claims form/837 billing form
- Patient level diagnoses / procedures, and provider specialties
- Sourced by retail, mail order and specialty pharmacies across the U.S. through the NCPDP form
- Prescription details (drug brand/generic name, quantity, days supply) and prescriber/pharmacy data



## U.S. NET Phase Ib bridging study



Encouraging surufatinib efficacy in everolimus & sunitinib refractory/intolerant patients





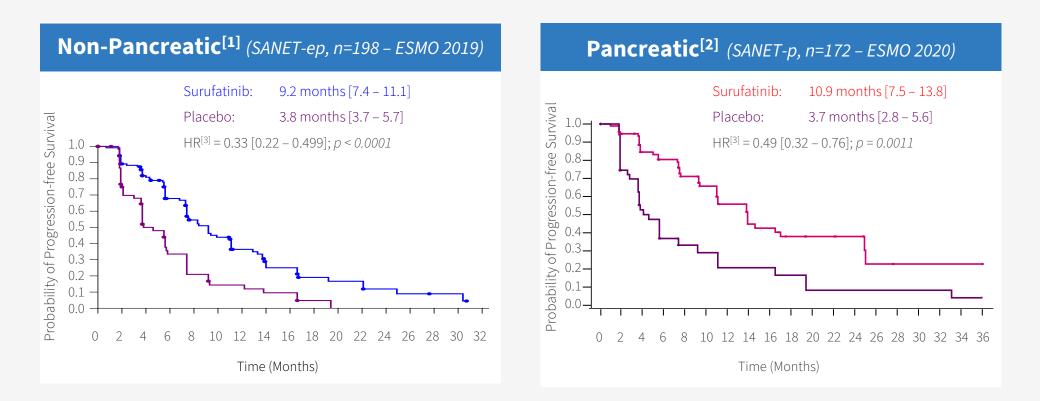
### Similar PK and Toxicity Profile between China & U.S. patients

- 300mg QD recommended in both populations;
- PK: C<sub>max</sub> & AUC<sub>tau</sub> <10% difference; no meaningful impact of race on exposure;
- Safety: similar dose intensities; U.S. adverse events at or below China patients.

Data cut-off as of April 21, 2020.

# Surufatinib: Monotherapy efficacy across NETs HUTCHMED

- >950 patients in clinical trials to date
- Proven single-agent efficacy: SANET-ep & SANET-p Phase IIIs met endpoints at interim

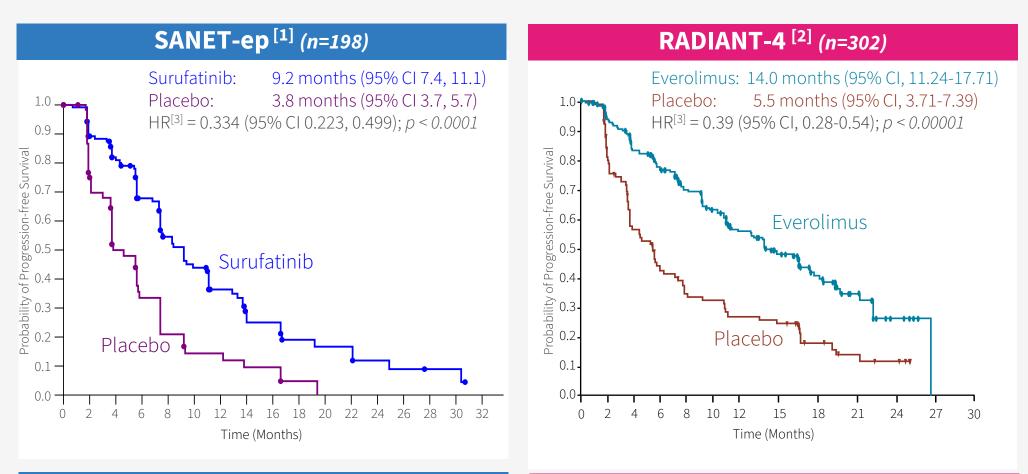


[1] Xu J, Shen L, Zhou Z, et al. Surufatinib in advanced extrapancreatic neuroendocrine tumours (SANET-ep): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1500-1512. doi:10.1016/S1470-2045(20)30496-4; [2] Xu J, Shen L, Bai C, et al. Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1489-1499. doi:10.1016/S1470-2045(20)30493-9; [3] P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; Cl, confidence interval; HR, hazard ratio.

## G1/2 Advanced extra-pancreatic NET



### Investigator assessed median PFS



### SANET-ep Primary (1°) endpoint was Investigator mPFS BIIRC <sup>[4]</sup> mPFS for supportive analysis not 1° or 2° endpoint

### RADIANT-4 Primary (1°) endpoint was BIIRC <sup>[4]</sup> mPFS Investigator mPFS not 1° or 2° endpoint

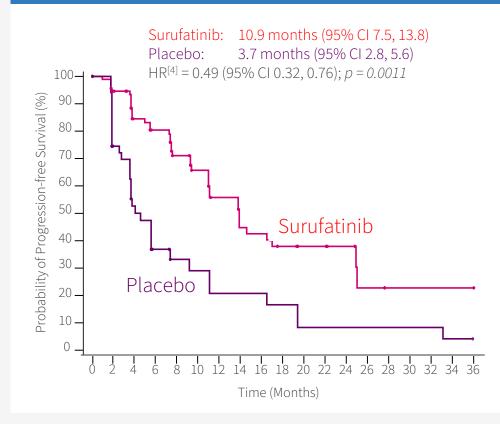
[1] Xu et al. "Surufatinib in advanced extrapancreatic neuroendocrine tumours (SANET-ep): a randomised, double-blind, placebo-controlled, phase 3 study." Lancet Oncol 2020. Published online September 20, 2020. https://doi.org/10.1016/S1470-2045(20)30496-4; [2] Yao et al. "Everolimus for the treatment of advanced, non-functional neuroendocrine tumors of the lung or gastrointestinal tract (RADIANT-4)" Lancet. 2016 Mar 5;387(10022):968-977. doi: 10.1016/S0140-6736(15)00817-X. Epub 2015 Dec 17; [3] P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; CI, confidence interval; HR, hazard ratio; [4] BIIRC = Blinded Independent Image Review Committee (Central).

# G1/2 Advanced pancreatic NET



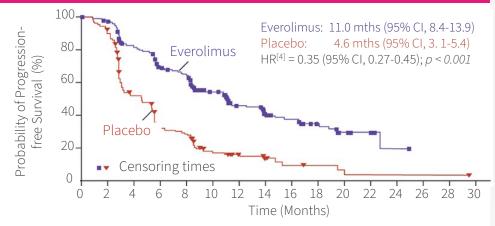
### Investigator assessed median PFS (primary endpoints)

### **SANET-p**<sup>[1]</sup>(*n*=172)

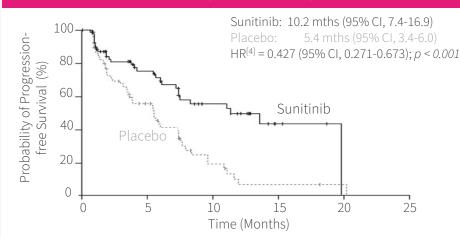


 Xu et al. "Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebocontrolled, phase 3 study." Lancet Oncol 2020. Published Online September 20, 2020 https://doi.org/10.1016/S1470-2045(20)30493-9; [2] Yao et al. Everolimus for advanced pancreatic neuroendocrine tumors" N Engl J Med. 2011;364(6):514–23 DOI: 10.1056/NEJMoa1009290; [3] Raymond et al. Sunitinib malate for the treatment of pancreatic neuroendocrine tumors [published correction appears in N Engl J Med. 2011 Mar 17;364(11):1082]. N Engl J Med. 2011;364(6):501-513 DOI: 10.1056/NEJMoa1003825;
 P-value from SANET-p is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; Cl, confidence interval; HR, hazard ratio.

RADIANT-3 (everolimus) <sup>[2]</sup> (n=410)



### A6181111 (sunitinib) [3] (n=171)



## Surufatinib vs. everolimus and sunitinib



## Broader range of tumor origins & later-stage patients

		Asia/China Extra-	SANET-ep <sup>[1]</sup> (n=198)		U.S. Extra-	<b>RADIANT-4</b> <sup>[2]</sup> ( <i>n</i> =302)	<b>SANET-ep</b> Enrolled more pts with poor prognosis.
		Pancreatic NET	(surufatinib vs placebo)		Pancreatic NET	(everolimus vs placebo)	Survival
		Tsai et al. 2013			Yao et al. 2008		Primary Site mOS Rate @ 5-yr
	Gastrointestinal Tract	58%	47%	Gastrointestinal Tract	50%	58%	Rectum 2.8y 28%
	Rectum	30%	27%	Rectum	33%	13%	
Non-Pancreatic	Stomach	7%	10%	Stomach	8%	4%	Small Intestine 8.6y 69%
	Small Intestine	19%	8%	Small Intestine	6%	34%	
Tumor Origin	Other GI	3%	3%	Other GI	4%	7%	RADIANT-4
	Lung	22%	12%	Lung	21%	30%	Did not enroll other extra-pancreatic
	Other Organ Site		<b>28%</b> 7%	Thymus		1%	
	Thymus Liver		6%				NET organ sites incl. but not limited to
	Mediastinum		6%				Thursday Thursday
	Adrenal Gland		2%				Throat Thyroid Kidney Ovary SANET-ep
	Other		8%				Mediastinum Adrenal gland
	Unknown Origin		14%	Unknown Origin		12%	Retroperitoneal Ampulla vater <b>Broader pt.</b>
	NON-PA	NCREAT	IC NET	PAN	CREATIC		Parathyroid Carotid body coverage.
		<b>SANET-ep</b> <sup>[1]</sup> ( <i>n</i> =198)	<b>RADIANT-4</b> <sup>[2]</sup> ( <i>n</i> =302)	SANET-p <sup>[3]</sup> (n=172)	<b>RADIANT-3</b> <sup>[4]</sup> ( <i>n</i> =410)	<b>A6181111</b> <sup>[5]</sup> (n=171)	
Pathology grado	Grade 1	16%	65%	12%	83%	n/a	
Pathology grade	Uraue z	84%	35%	88%	17%	n/a	
ECOG PS 0:1	PS 0 (treatment : control)	60% (56% : 67%)	74% (73% : 75%)	67% (65% : 73%)	66% (67%: 66%)	55% (62% : 48%)	Surufatinib Later-stage patients, more heavily
	<b>PS 1</b> (treatment : control)	40% (44% : 33%)	26% (27% : 26%)	33% (35% : 27%)	31% (30%:32%)	44% (38%:51%)	pre-treated (incl. with targeted
	Any Prior Treatment	67%	61%	66%		69%	therapy) & weaker physical status.
Prior systemic	Chemotherapy	40%	25%	26%	50%	66%	Likely due to later diagnosis in China &
treatment	Targeted therapy	10%	none	9%	none	none	availability of everolimus.
	Somatostatin Analogues	32%	55%	44%	50%	36%	
Number of	≤2	34%	n/a	49%	64%	64%	
organs involved	≥3 or unknown	66%	n/a	51%	36%	36%	

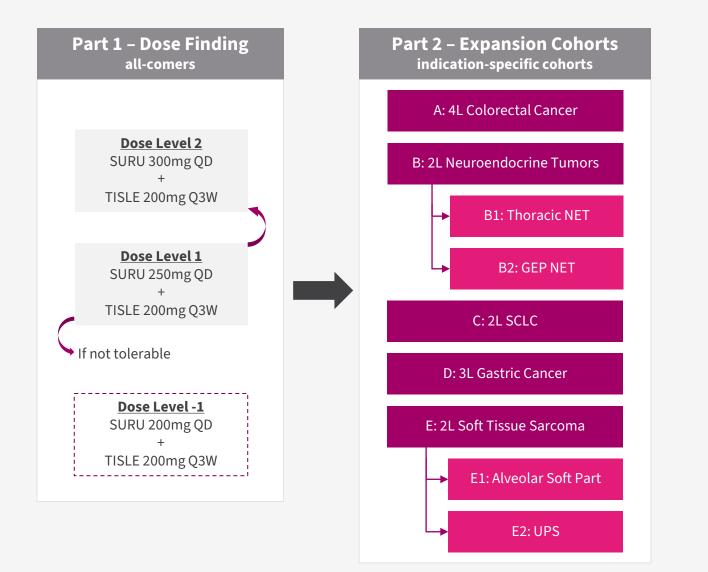
Source: Yao et al, Lancet 2016 387(10022) 968-77; Yao et al, JAMA Oncol 2017 3(10) 1335-42; Excludes 7% pancreatic NET in U.S. series and 6% in Asia series;

Colon-rectum in Tsai et al. (2013) report; Colon approximately 8% in Asian series (Shebani KO et al. (1999)); Colon-rectum in Yao et al. (2008) report; Colon approximately 4-7% in U.S./E.U. series (Niederle B et al. (2016))

[1] Xu et al. https://doi.org/10.1016/S1470-2045(20)30496-4; [2] Yao et al. doi: 10.1016/S0140-6736(15)00817-X; [3] Xu et al. https://doi.org/10.1016/S1470-2045(20)30493-9; [4] Yao et al. DOI: 10.1056/NEJMoa1009290; [5] Raymond et al. DOI: 10.1056/NEJMoa1003825

## Surufatinib PD-1 combos global aspirations

## Surufatinib + Tislelizumab (PD-1 mAb) first patient enrolled in March 2021



### Rationale

HUTCHM

- Global aspirations
- Global PD-1 partner
- May lead to accelerated opp given high unmet need

### **Status**

- Part 1 enrolling rapidly
- Multiple U.S. sites active
- E.U. site pending activation in Part 2

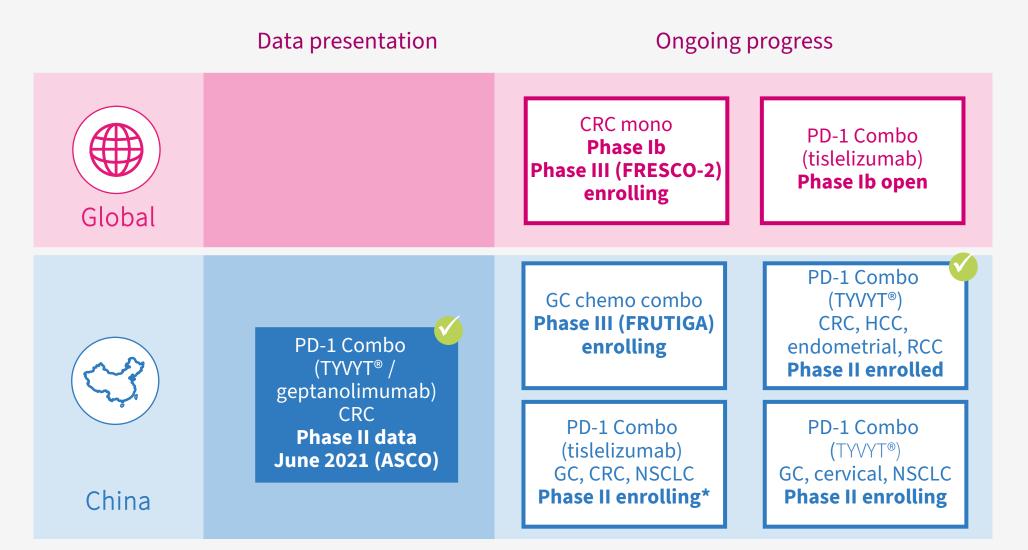


# A3c

## FRUQUINTINIB (ELUNATE<sup>®</sup> IN CHINA)

A highly selective small molecule inhibitor of VEGFR 1/2/3 designed to improve kinase selectivity to minimize off-target toxicity and thereby improve tolerability

## Fruquintinib clinical development updates



litette

HUTCHMED

## Fruquintinib & surufatinib both unique VEGFR TKIs



### ...potentially ideal VEGFR combos for immunotherapy

ТКІ	1st Generation			2nd Generation			Next Generation		
Selectivity	Multiple targets			Relatively selective			Highly selective	Selective angio-immuno kinase inhibitor	
Inhibitors	Sutent®	Nexavar®	Focus V®	Fotivda®	Lenvima®	Inlyta®	Fruquintinib	Surufatinib	
Status	Launched	Launched	Launched	Launched	Launched	Launched	Launched	Approved	
VEGFR1 (nM)	2	26	27	30	22	3	33	2	
VEGFR2 (nM)	9	90	0.2	6.5	4	7	25	24	
VEGFR3 (nM)	19	20	0.7	15	5	1	0.5	1	
Phos-KDR (nM)	10	30	0.1-1	0.16	0.8	0.2	0.6	2	
Other kinases (IC50 < 100nM)	PDGFRα PDGFRβ c-Kit Flt3 Ret CSF-1R	Raf-1 b-raf Flt3 P38 c-Kit Ret	PDGFRα PDGFRβ FGFR1-4 c-Kit	PDGFRα PDGFRβ EphB2 c-Kit Tie2	PDGFRα PDGFRβ FGFR1-4 Ret c-Kit	PDGFRα PDGFRβ c-Kit	none	CSF-1R FGFR1 FLT3 TrkB	
First Patent Expiration			Apr 2027 / Nov 2028 (with PTE)	2021/10/19 (US7253286B2)	2025/04/29 (US6534524B1)	2029 (without extension)	2030 (without extension)		

- **Fruquintinib is uniquely selective** unlike other TKIs with off-target toxicity
- Surufatinib inhibits TAM<sup>[1]</sup> production amplifying PD-1 induced immune response

## Efficacy advantage



	FRESC	O <sup>[1]</sup>	CON	CUR	CON	ICUR	CORR	ECT	
Third-Line Metastatic Colorectal cancer	Mainland China		(Mainland C	Chinese Patients (Mainland China, Hong Kong, Taiwan) <sup>[2]</sup>		Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		Global	
Treatment arms	<b>ELUNATE</b> ®	Placebo	STIVARGA®	Placebo	STIVARGA®	Placebo	STIVARGA®	Placebo	
Patients (n)	278	138	112	60	136	68	505	255	
Objective Response Rate, n (%)	4.7%	0.0%	3.6%	0.0%	4.4%	0.0%	1.0%	0.4%	
Disease Control Rate, n (%)	62.2% +49	.9 12.3%	45.5% +38	.8 6.7%	51.5%	-44.1 7.4%	41.0% +2	6.1 14.9%	
Median Progression-Free Survival (mPFS) (mo.)	3.7 +1	. <mark>9</mark> 1.8	2.0 +0.	<sup>3</sup> 1.7	3.2	+1.5 1.7	1.9 +(	0.2 1.7	
						100	% AVASTIN® prior use	×	
Median Overall Survival (mOS) (mo.)	9.3 +2	.7 6.6	8.4 +2.2	2 6.2	8.8	+2.5 6.3	6.4 +	1.4 5.0	
<ul> <li>Advantage for ELUNATE<sup>®</sup> efficacy vs.</li> <li>Stivarga<sup>®</sup> in Chinese metastatic CRC p</li> </ul>	ots;						Hazard Ratio (95% CI)	p-value	
⟨𝔅⟩ Advantage for ELUNATE <sup>®</sup> post	Overal	l					0.65 (0.51, 0.83	) <0.001	
VEGF/EGFR targeted therapy	with pr	ior anti-VEGF	therapy			+	0.68 (0.45, 1.03)	0.066	
• mOS: 7.69 mo. vs. 5.98 mo. placebo	withou	t prior anti-V	EGF therapy			1	0.60 (0.45, 0.80)	< 0.001	
(HR 0.63 & p-value 0.012) • mPFS: 3.65 mo. vs. 1.84 mo. placebo	with pr	ior anti-VEGF	or anti-EGFR th	erapy			0.63 (0.46, 0.90)	0.012	
(HR 0.24 & p-value < 0.001)		t prior anti-V	EGF or anti-EGFF	R therapy		1	0.63 (0.43, 0.86)	0.003	
				<b>*</b>	0.5	1.0 1.5	2.0		

Favors Fruquintinib Favors Placebo

[1] Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial; [2] Efficacy & safety of regorafenib monotherapy in Chinese patients with previously treated metastatic colorectal cancer: subgroup analysis of the CONCUR trial; R Xu.

## Stivarga<sup>®</sup> tox limitations



	ELUNATE®	Stivarga® (regorafenib) tablets
<b>BIOCHEMICAL ACTIVITY</b>	IC <sub>50</sub> (nmol/L)	IC <sub>50</sub> (nmol/L)
On-Target Kinases:		
VEGFR1	33	13
VEGFR2	35	4.2
VEGFR3	0.5	46
Off-Target Kinases:		
Ret	128	1.5
FGFR1	181	202
c-kit	458	7
PDGFRβ	>10,000	22
RAF-1	>10,000	2.5
B-RAF	>10,000	28
B-RAF <sup>V600E</sup>	>10,000	19

#### Stivarga<sup>®</sup> liver toxicity black-box warning:

→ Increased liver function test monitoring (weekly if elevated) & remedial dose interruption.

#### STIVARGA (regorafenib) tablets, oral Initial U.S. Approval: 2012

#### WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning.

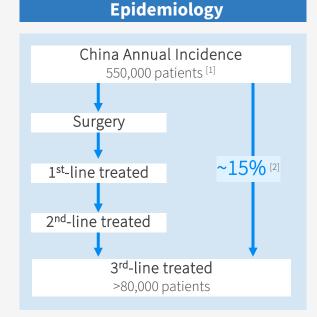
- Severe and sometimes fatal hepatotoxicity has been observed in clinical trials. (5.1)
- Monitor hepatic function prior to and during treatment. (5.1)
- Interrupt and then reduce or discontinue Stivarga for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence. (2.2)

		NATE <sup>®</sup> nib Capsules		<b>/arga®</b> enib) tablets	
3 <sup>rd</sup> -Line Metastatic Colorectal cancer	FRESCO Mainland		CONCUR Study (Mainland China, HK, Taiwan) <sup>[2]</sup>		
Treatment arms	<b>ELUNATE</b> ®	Placebo	<b>STIVARGA®</b>	Placebo	
Patients (n)	278	138	112	60	
≥G3 AE (Safety population)	61.1%	19.7%	69.6%	46.7%	
SAE (Safety population)	15.5%	5.8%	31.3%	26.7%	
VEGFR on-target related AEs:					
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%	
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%	
Off-target (i.e. non-VEGFR) related AEs:					
Hypophosphatemia, ≥G3	0.0%	0.0%	8.0%	0.0%	
Hypokalemia, ≥G3	0.7%	0.7%	6.3%	0.0%	
Rash/desquamation, ≥G3	0.0%	0.0%	4.4%	0.0%	
Lipase increase, ≥G3	0.0%	0.0%	6.3%	1.7%	
Hepatic function (Liver function) AEs:					
ALT increased, ≥G3	0.7%	1.5%	7.1%	3.3%	
AST increased, ≥G3	0.4%	0.7%	8.9%	0.0%	
Blood bilirubin increased, ≥G3	1.4%	1.5%	8.9%	8.3%	
Tolerability:					
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%	
AE Leading to dose reduction	24.1%	4.4%	23.2%	0.0%	
AE Leading to treatment discontinuation	15.1%	5.8%	14.3%	6.7%	

### ELUNATE<sup>®</sup> superior safety – advantage especially for liver mets patients

## NRDL

## 2020 accessible pricing



#### 2020 estimated penetration:

- ~39,500 cycles used (OOP & PAP);
- Average 4.7 months per patient;
- ~8,400 patients paid for ELUNATE<sup>®</sup>;
- Representing ~10% penetration.



### National Reimbursement Drug List (NRDL)

#### Effective Jan 1, 2020: 8 newly listed oncology drugs, including ELUNATE<sup>®</sup> NRDL reimburses 50-70% of patient costs under urban scheme Without Medical With Medical Costs per cycle (all US\$)<sup>[3]</sup> Insurance Insurance **ELUNATE**<sup>®</sup> Pre-NRDL (without PAP) 3,260 3,260 (fruquintinib) Post-NRDL 1,180 1,180 3L CRC Pts Out-of-~350 [5] ~1,180 Pocket Cost STIVARGA<sup>®</sup> 3L CRC Pts Out-of-~670 [5] ~2,220 (regorafenib) Pocket Cost

# Fruquintinib: U.S. CRC Landscape Overview<sup>[1]</sup>

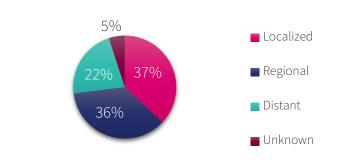
### Approved Stivarga (rego) & Lonsurf (TAS-102) used 20% to 30% in 3L+ patients Unmet need remains high in refractory setting

### **CRC Current and Future Market Situation**

- Total value of CRC market expected to increase from \$4.7bn in 2016 to \$7.5bn in 2025 (U.S., JPN and E.U.5)<sup>[2]</sup>
- U.S. CRC market value growing from \$2.0bn in 2016 to \$3.5bn in 2025 (CAGR = 6.4%) due to high prevalence of CRC in the U.S. and uptake of new targeted therapies <sup>[2]</sup>
- Est. 149,500 CRC new cases diagnosed in U.S., 2021
  - 32,890 (or 22%) are metastatic at diagnosis
  - >67K patients treated for mCRC in 2018



### Percent of Cases by Stage at Diagnosis<sup>[3]</sup>



HUTCHN

#### **Fast Evolving Treatment Landscape**

- Chemotherapy, anti-VEGF, and anti-EGFR agents to continue as mainstay of treatment, novel MoAs provide more treatment options
  - Stivarga (regorafenib) and Lonsurf (TAS-102): SoC for 3L treatment
  - Stivarga: approved by the FDA with a liver toxicity black box warning: severe and sometimes hepatotoxicity observed
- Increasing number of options, treatment beyond 3<sup>rd</sup> line likely to increase

#### **Unmet needs and challenges**

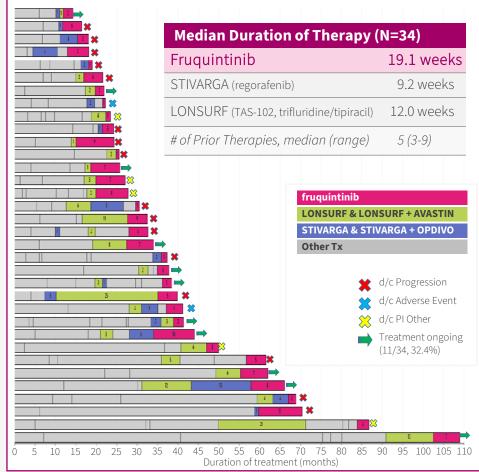
- Novel treatment options available for rarer subtypes; larger subsets are treated with traditional options
- Lack of treatment options that can significantly improve prognosis for metastatic patients
  - 5-year survival rate for mCRC remains only slightly over 14%
- Unmet Medical Need remains high for 4L and beyond
  - Fruquintinib shown strong data already in CRC 3L and beyond
  - Limited strategies for managing drug resistance

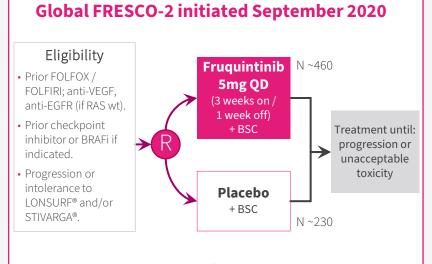
# **U.S. data supporting FRESCO-2 initiation**



AACR, ASCO & ESMO presentations demonstrate compelling preliminary monotherapy efficacy and safety in heavily pre-treated U.S. CRC patients

### U.S. Ph. Ib: 81% stable disease in evaluable pts (ESMO'20)





#### ~150 sites in 14 countries incl. U.S., Europe, Japan & Aus. ~690 pts full enrollment targeted to complete late 2021

• Interim futility analysis at 1/3 (160) OS events.

#### Primary Endpoint: OS in refractory mCRC pts Secondary Endpoints: PFS, ORR, DCR, DoR, QoL, others

#### Stratification factors:

- Prior TAS-102 vs. prior regorafenib vs. prior TAS-102 & regorafenib.
- RAS status (WT vs MT).
- Duration of metastatic disease (≤18 mths vs > 18 mths).

#### Data cut-off as of Aug 20, 2020.

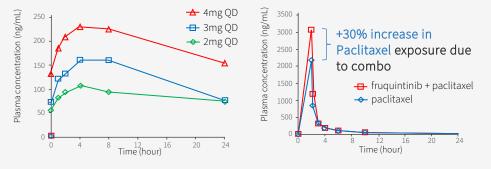
[1] Dasari, et al. Phase 1/1b Trial of Fruquintinib in Patients with Advanced Solid Tumors: Preliminary Results of the Dose Expansion Cohort in Refractory mCRC. ESMO 2020 Abstract #2217; [2] Li J, Qin S, Xu R, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. JAMA. 2018;319(24):2486–2496. doi:10.1001/jama.2018.7855.

## Gastric combo with paclitaxel

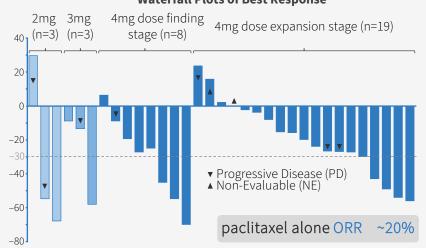


### Phase 2 results supports ongoing Phase III FRUTIGA

Dose proportional increase of fruquintinib AUC at steady state. 30%+ increase in paclitaxel exposure (mean AUC<sub>0-8</sub>) after multiple dose fruquintinib.



#### 2 ORR of 36% (10/28) & DCR of 68% in efficacy evaluable pts. Fruquintinib 4mg, ≥16 wk. PFS of 50% & ≥7 mo. OS of 50%.



Waterfall Plots of Best Response

3 Encouragingly low level of dose reduction/interruption. Actual mean administered dose in the first cycle was 3.32mg/day for fruquintinib (83.0% planned dose) & 78.6 mg/m2/week for paclitaxel (98.3% planned dose).

Characteristics (Unit)	Drug Expansion Stage (N=19) Fruq. 4 mg + paclitaxel 80 mg/m²		
	Drug interruption	Drug reduction	
Dose modification with Fruquintinib N (%)	2 (10.5%)	2 (10.5%)	
Dose modification with Paclitaxel N (%)	5 (26.3%)	1 (5.3%)	

AE profile in-line with expectations. Neutropenia – a paclitaxel AE – with 57.9% Grade >3 AEs. Similar to 60% seen ramcirumab (VEGF mAb) RAINBOW study paclitaxel combo in 2L gastric.

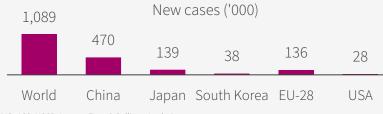
Drug related grade 3 or 4 AEs (NCI-CTCAE v 4.0) term	Dose Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m²
Neutropenia	11 (57.9%)
Leukopenia	4 (21.0%)
Hypertension	2 (10.6%)
PLT decreased	1 (5.3%)
Anemia	1 (5.3%)
HFSR	1 (5.3%)
Mucositis oral	1 (5.3%)
Hepatic disorder	1 (5.3%)
Upper gastrointestinal hemorrhage	1 (5.3%)

# FRUTIGA – 2L gastric combo with paclitaxel



Ongoing - interim futility analysis Jun 2020 (~200 OS events)

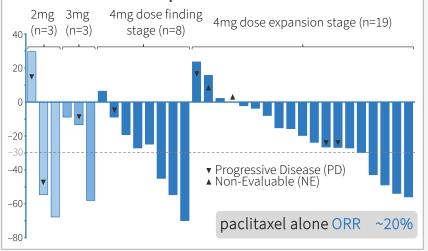
Gastric (stomach) cancer is the 5<sup>th</sup> most common cancer globally –769,000 deaths/year



WHO, ACS, NCCR, Lancet, Frost & Sullivan Analysis.

### Ph Ib ORR of 36% & DCR of 68% in evaluable pts. 4mg: $\geq 16$ week PFS of 50% & $\geq 7$ mo. OS of 50%.

#### Waterfall Plots of Best Response



#### **FRUTIGA study design** Patient eligibility Fruquintinib 4mg QD 3/1 + paclitaxel 80mg/m<sup>2</sup>, D1, D8, D15 Gastroesophageal 28-day per cycle junction or gastric Treatment until: cancer progression or Progressed after unacceptable 1<sup>st</sup> line chemo w/ toxicity or withdrawal fluoropyrimidine Placebo + & platinum paclitaxel 80mg/m<sup>2</sup>, D1, D8, D15 N=700 28-day per cycle

Tumor response assessment every 4 weeks during first 3 cycles, every 8 weeks thereafter per RECIST v1.1

### Primary endpoint: OS Secondary endpoints: PFS, ORR, DCR, DoR, QoL Enrollment targeted to complete around YE 2021

- \*Stratified factors:
- GEJ vs GC;
- Peritoneal metastasis Y or N;
- ECOG PS 0 vs 1

# FALUCA – Third-line NSCLC Monotherapy

# HUTCHMED

### Presented at WCLC 2019

### FALUCA Phase III (enrolled Dec 2015 to Feb 2018)

- <u>Met all</u> secondary endpoints: mPFS; ORR; DCR; & DoR <sup>[1]</sup>;
- Did not achieve primary endpoint of median OS, however:
  - Anti-tumor therapies after disease progression reduced OS diff.
  - Higher percentage of placebo pts received subsequent treatments.

## Significant difference in subsequent anti-tumor treatments (ATT)

- Chemotherapy: Fruq. 29.7% vs. Placebo 53.8%
- Targeted therapies (VEGFi and/or EGFRi): Fruq. 20.9% vs. Placebo 31.2%
- TAGRISSO<sup>®</sup> & anlotinib just approved in 2017

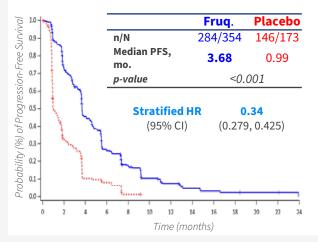
#### Efficacy Endpoints (Intent-to-Treat) [2]

	Fruq. (N=354)	Placebo (N=173)	p-value
mOS (mths)	8.94	10.38	0.841
mPFS (mths)	3.68	0.99	<0.001
ORR	<b>13.8%</b> (49)	0.6% (1)	<0.001
DCR	<b>66.7%</b> (236)	24.9% (43)	<0.001

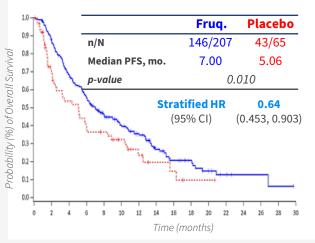
#### Good safety; most Grade ≥3 TEAEs targetrelated & clinically manageable.

8	
Fruq. (N=354)	Pbo (N=173)
216 (61.2%)	47 (27.6%)
37 (10.5%)	9 (5.3%)
61 (17.3%)	7 (4.1%)
85 (24.1%)	2 (1.2%)
74 (21.0%)	5 (2.9%)
39 (11.0%)	0
	Fruq. (N=354) 216 (61.2%) 37 (10.5%) 61 (17.3%) 85 (24.1%) 74 (21.0%)

#### **PFS in ITT population**



#### OS in pts w/o subsequent ATT



[1] mOS = median Overall Survival; mPFS = median Progression-Free Survival; ORR = Objective Response Rate; DCR = Disease Control Rate; DoR = Duration of Response; HR = hazard ratio; 95% CI = 95% Confidence Interval; [2] Lu, et al. "A Randomized Phase III trial of Fruquintinib versus Placebo in Patients with Advanced Non-Small Cell Lung Cancer (FALUCA)." WCLC 2019 Abstract #MA14.05; [3] Lu, et al. Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase II Study of Fruquintinib After Two Prior Chemotherapy Regimens in Chinese Patients With Advanced Non-Small-Cell Lung Cancer. Journal of Clinical Oncology 36, no. 12 (April 20 2018) 1207-1217. DOI: 10.1200/JCO.2017.76.7145; [4] Li, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. JAMA. 2018 Jun 26;319(24):2486-2496. doi: 10.1001/jama.2018.7855. \* Post-hoc analysis.





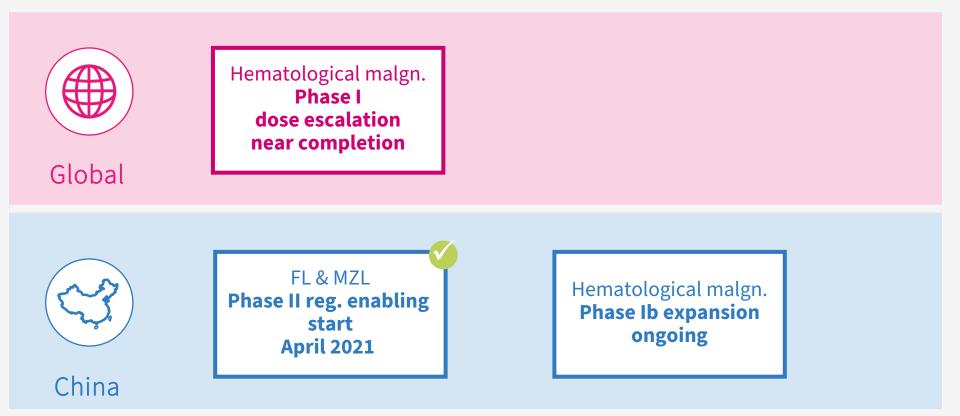
## HMPL-689 & HMPL-523

Targeting B-cell signaling for hematological cancers and immunology

## HMPL-689 clinical development updates



**Ongoing progress** 



## HMPL-689 – finding major room for improvement



### Safety profiles of current PI3K $\delta$ inhibitors are not good

PI3K $\delta$  inhibitors being developed in a broad range of indications.

Compound	Company	Indication	Status	Issue	
Zydelig <sup>®</sup> idelalisib – ΡΙ3Κδ	Gilead	Relapsed CLL/SLL, FL	Approved	<b>BOXED WARNING</b> : FATAL AND SERIOUS TOXICITIES: HEPATIC, SEVERE DIARRHEA, COLITIS, PNEUMONITIS, INFECTIONS, and INTESTINAL PERFORATION	
e		Relapsed or refractory CLL/SLL	Approved	BOXED WARNING: FATAL AND SERIOUS TOXICITIES:	
Copiktra <sup>®</sup> duvelisib – ΡΙ3Κγ/δ	Secura Bio/ CSPC <sup>[2]</sup>	Relapsed or refractory FL	Approved <sup>[1]</sup>	INFECTIONS, DIARRHEA OR COLITIS, CUTANEOUS REACTIONS, and PNEUMONITIS	
		Peripheral T-cell lymphoma	Phase II enrolling	Need to spare PI3Ky	
Aliqopa <sup>®</sup> copanlisib – ΡΙ3Κα/δ	Bayer	Relapsed FL	Approved <sup>[1]</sup>	Gastrointestinal and liver AEs including hyperglycemia, diarrhea, hypertension, leukopenia, neutropenia, nausea and thrombocytopenia	
		Previously treated MZL	Approved <sup>[1]</sup>		
Ukoniq® Umbralisib - ΡΙ3Κδ	TG Therapeutics	Previously treated FL	Approved <sup>[1]</sup>	Gastrointestinal & liver AEs	
	merapeaties	Previously treated NHL, CLL	Phase IIb/III		
		FL, MZL, MCL	NDA filing H2-2021	Pending 12 months follow-up data from last responder [3]	
Parsaclisib <sub>Ρι3κδ</sub>	Incyte/ Innovent	Refractory myelofibrosis	Phase III	Phase 2 studies required prophylaxis for pneumocystis	
PISKO	(o innovent	Autoimmune hemolytic anemia	Phase II	jirovecii pneumonia (PJP)	
Zandelisib	, ,	Relapsed or refractory FL	Phase II (for pot. AA)	Progressing with intermittent dosing to mitigate immune related toxicities; all patients underwent prophylaxis for	
ΡΙ3Κδ	Hakko Kirin	B-Cell Malignancies	Phase I/Ib	pneumocystis jirovecii pneumonia (PJP) [4]	

CLL/SLL: chronic lymphocytic leukemia/small lymphoma; **HL**: follicular lymphoma; **MZL**: marginal zone lymphoma; **MCL**: mantle cell lymphoma; **DLBCL**: diffuse large B cell lymphoma; **HL**: Hodgkin's lymphoma; **NHL**: non-Hodgkin's lymphoma.

(1) Accelerated approval was granted based on ORR, continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trials; [2] AbbVie ended collaboration with Infinity in June 2016 following Phase II results in indolent non-Hodgkin's lymphoma. Duvelisib licensed to Verastem in November 2016, who subsequently sold the asset to Secura Bio in September 2020; [3] company announcement Dec 7, 2020; [4] ASCO 2020 Abstract #8016.

## HMPL-689 – designed to be better

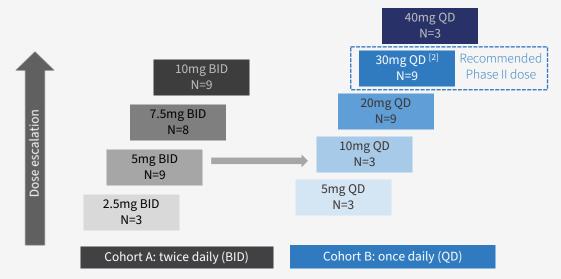


### Intent to improve safety...

### HMPL-689 – Advantages

- Improved isoform selectivity sparing PI3Kγ & PI3Kα.
- Improved potency at whole blood level over five-fold more potent than Zydelig<sup>®</sup> to cut compound related toxicity.
- Improved PK properties particularly efflux & drug/drug interaction due to CYP inhibition / induction, critical for combo therapy.

#### **Dose escalation schema**



#### Manageable toxicity profile [1]

	All grade 43% 29% 27% 25% 21%	Grade ≥3 11% 4% 2% 16% 2%
eukopenia LT increased neumonia	29% 27% 25%	4% 2% 16%
LT increased neumonia	27% 25%	2% 16%
neumonia	25%	16%
	2070	1070
ST increased	21%	204
		2%0
ipase increased	20%	5%
ough	18%	-
nemia	16%	-
lood bilirubin increased	16%	2%
louth ulceration	14%	-
yrexia	14%	-
Ipper respiratory tract infection	14%	-
ilirubin unconjugated increased	13%	2%
sthenia	11%	-
lood creatinine increased	11%	-
onstipation	11%	-
lyperglycemia	11%	-

### HMPL-689: Clinical profile being confirmed

### China-based Phase Ib dose expansion cohorts enrolling to inform registration studies

#### Dose expansion

30~40 pts for each cohort

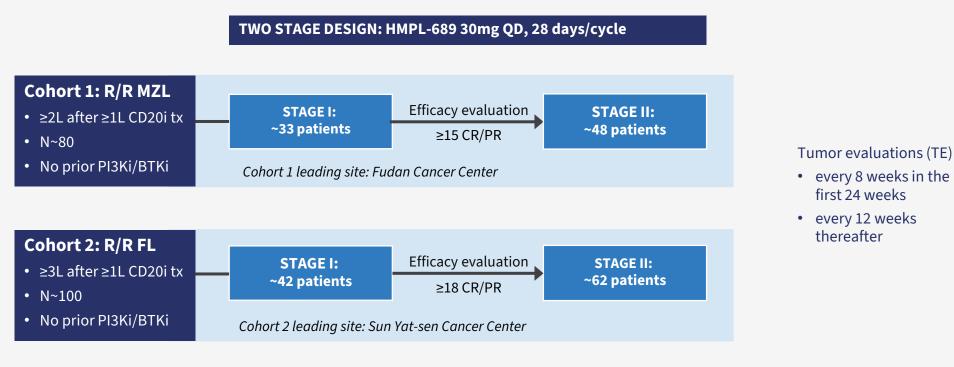
A: 2L+ MZL	• Expansion completed – registration intent Phase II initiated
B: 3L+ CLL/SLL	Expansion continuing to enroll
C: 3L+ FL (stage 1,2,3a)	• Expansion completed – registration intent Phase II initiated
D: MCL, DLBCL, FL(3b)	Expansion continuing to enroll
E: T-cell lymphoma	Expansion continuing to enroll

Treatment until unacceptable tox, disease progression or withdrawal of consent

**Primary endpoint:** ORR **Secondary endpoints:** PFS, TTR, DoR, PK HUTCH

### HMPL-689: China registration intent Phase II

#### First patient enrolled April 2021



• Primary efficacy endpoint IRC-assessed ORR

• Secondary efficacy endpoints IRC-assessed CRR, PFS, CBR, TTR, and DoR; Invassessed ORR, CRR, PFS, CBR, TTR, DoR, and OS

- Full enrollment targets
  - FL by H1 2022
  - MZL by H2 2022

HUTCH

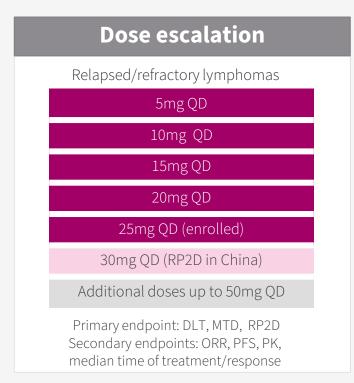
### HMPL-689: U.S./E.U. Lymphoma Phase Ib

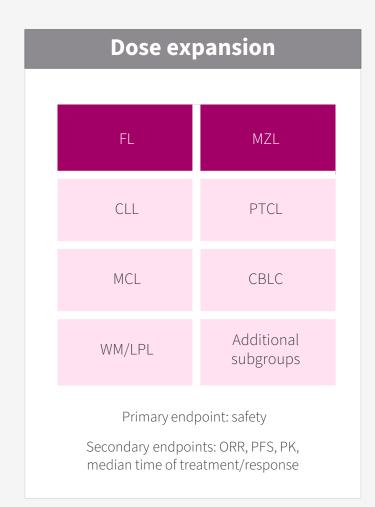


#### Intl to build on China data, and engage FDA in H2 2021

#### Next step: Complete dose escalation in Q3 2021

- Dose expansion to focus on FL and MZL
- End of Phase I meeting with U.S. FDA H2 2021 to confirm registration path

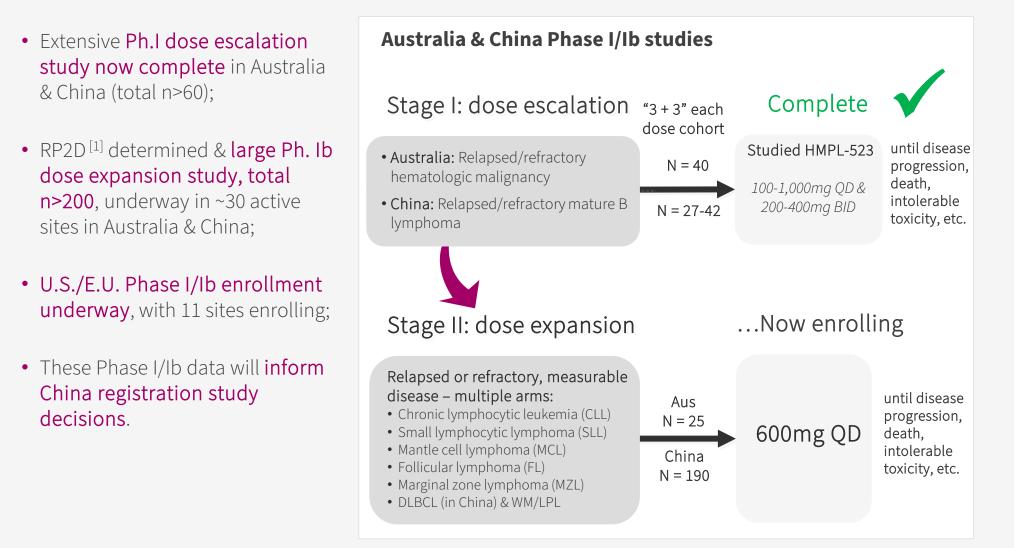




### HMPL-523 (Syk) in hematological cancer



#### Phase I/Ib ongoing in Australia, China, U.S. & E.U.



#### [1] RP2D = Recommended Phase II doses.

### HMPL-523 Global NHL Development Overview

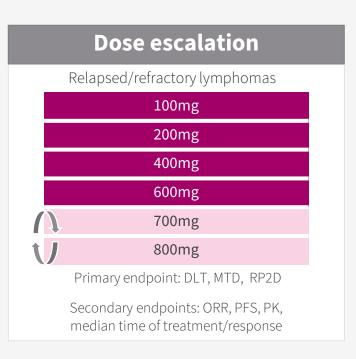


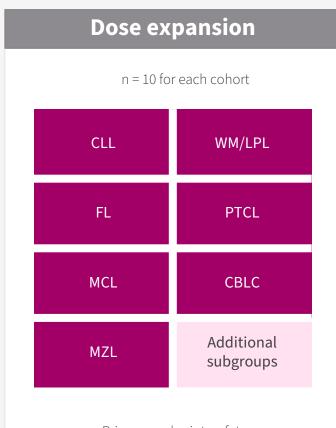
International to build on China data, and explore additional subgroups

#### Next step: Complete dose escalation in Q3 2021

#### Lymphoma study:

- Establish RP2D for international development
- International expansion cohorts to start
- Explore options to **enrich for post-BTKi** patients in the expansion phase





Primary endpoint: safety

Secondary endpoints: ORR, PFS, PK, median time of treatment/response

### HMPL-523: Immune thrombocytopenia (ITP)



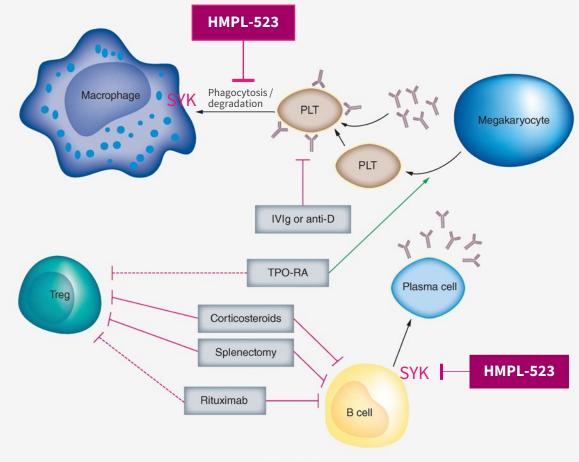
- Moderate efficacy
- All patients become refractory

#### SYK is a validated target for ITP

- Fostamatinib approved in the U.S.
- Moderate efficacy, dose limited by tox
- Syk targets both B cells & macrophages

#### **HMPL-523**

- China Phase II complete –encouraging efficacy and good safety
- Phase III planned to initiate late 2021



HUTCH

Adapted from Newland A, et al. Immunotherapy (2018) 10(1), 9–25





### **NEXT WAVE OF INNOVATIONS**

### What is next from discovery?



### Differentiated assets against multiple targets

### **Priming & activations**

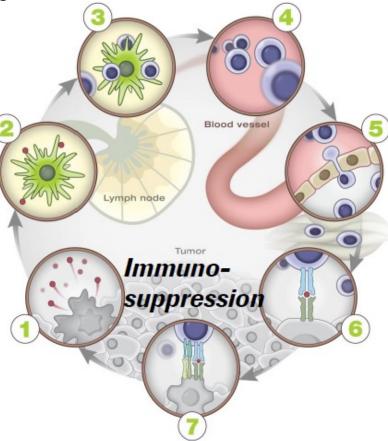
### Multiple mAb Programs

• HMPL-A83 (CD47)

#### **Antigen release**

- MET (savolitinib)
- EGFR (epitinib)
- Syk (HMPL-523)
- PI3Kδ (HMPL-689)
- FGFR (HMPL-453)
- IDH 1/2 (HMPL-306)
- ERK 1/2 (HMPL-295)
- BTK (HMPL-760)

# Multiple small molecule programs



### Anti-angiogenesis

- VEGFR (fruquintinib)
- VEGFR/FGFR (surufatinib)
- FGFR (HMPL-453)

### **Negative regulators**

- Treg (HMPL-689)
- CSF-1R (surufatinib, HMPL-653)

Multiple small molecule & mAb programs

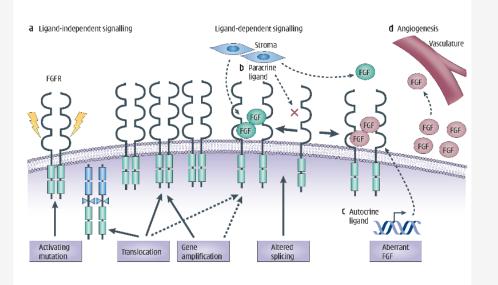
#### Creating highest-quality range of assets against novel targets for use in combos

### HMPL-453 – Phase II in China initiated



### Designed as best-in-class FGFR1/2/3 inhibitor

- 1. FGFR genetic alterations are oncogenic drivers.
- FGF/FGFR signaling normally involved in embryonic development, tissue repair, angiogenesis, neuroendocrine and metabolism homeostasis.
- Multiple oncogenic driver genetic alterations in FGFR pathway: gene amplification, mutation, translocation, fusion, splicing, etc.



## 2. FGFR – diverse & complicated genetic changes w/ multiple tumor types harboring low incidence.

	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7~15%) H&N squamous (10~17%) Esophageal squamous (9%) Breast (10~15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5~8%)
FGFR2	Gastric (5~10%) Breast (4%)	Intra-hepatic biliary tract cancer (cholangiocarcinoma) (14%) Breast (n/a)	Endometrial (12~14%) Lung squamous (5%)
FGFR3	Bladder (n/a) Salivary adenoid cystic (n/a)	Bladder (3~6%); Lung squamous (3%); Glioblastoma (3%) Myeloma (15~20%)	Bladder (60~80% NMIBC; 15~20 MIBC) Cervical (5%)

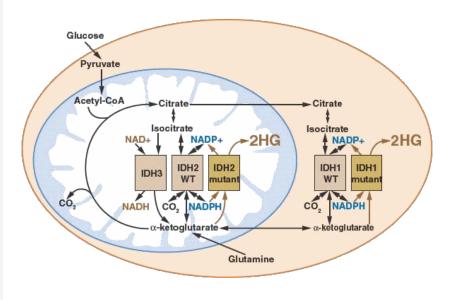
### Potential best-in-class IDH1/2 inhibitor



#### Potent IDH1/2 inhibitor with brain penetration

#### HMPL-306 is a potent IDH1/2 dual inhibitor

- IDH1 & 2 mutations are **validated targets** in R&R AML (IDH1i ivosidenib and IDH2i enasidenib)
- HMPL-306 provides **comparable efficacy** in preclinical model with **wider safety window**
- The higher penetration of blood-brain barrier with HMPL-306 makes exploring IDHm glioma attractive.



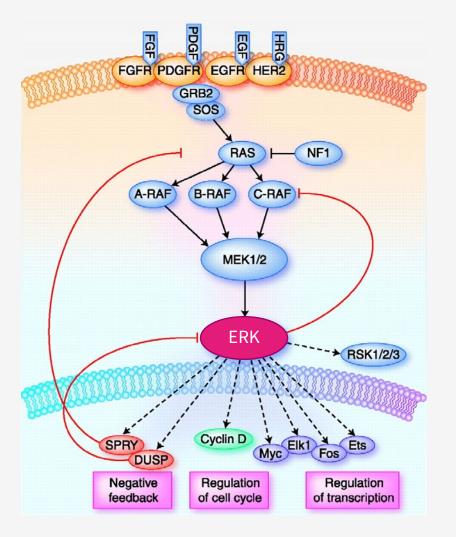
#### Unmet medical need & potential indications – IDH1/2 mutations are frequent genetic alterations in AML, glioma & solid tumors

TUMOR	%	IDH MU	TATION	[1]
	TOTAL	IDH1- R132	IDH2- R140	IDH2- R172
Brain tumor				
Grade 2 and 3 glioma	60-80%	60-80%	0%	1%
Secondary glioblastoma	70%	70%	0%	1%
Hematopoietic tumor				
Acute myelocytic Leukemia (AML)	15-25%	5-10%	5-15%	0-5%
Myelodysplastic syndrome (MDS)	10%	5%	5%	0%
Angioimmunoblastic T-cell lymphoma	26%	0%	1%	25%
Solid tumor				
Chondrosarcoma	55%	40%	0%	15%
Osteosarcoma	25%	0%	0%	25%
Cholangiocarcinoma	22%	20%	0%	2%
Giant cell tumors of bone	80%	0%	0%	80%

### MAPK pathway represents major unmet need



HMPL-295 – the first of several HUTCHMED assets targeting MAPK pathway



#### The MAPK (RAS-RAF-MEK-ERK) signaling cascade

- ERK (extracellular signal-regulated kinases) a key component
- *Pathway normal activation:* ligand-dependent & tightly regulated by NF-1 and negative feedback
- *In tumors:* activating mutations in RAS, RAF and loss of the tumor suppressor NF1 leads to uncontrolled cell proliferation

### ~50% of cancers associated with dysregulation in this pathway

- Increased mortality / poor OS
- Decreased the response to existing therapies including immunotherapy
- RAS: KRAS inhibitors in clinical trials
- BRAF/MEK: therapies approved induce initial rapid tumor regression, but acquire resistance developed due to MAPK pathway re-activation



# HUTCHMED

# INMAGENE Immunology partnership

# Accelerating four HUTCHMED drug candidates

#### Overview

- 4 novel preclinical drug candidates discovered by HUTCHMED for the potential treatment of multiple immunological diseases
- Funded by Inmagene
- Companies working together to move candidates to IND
- Inmagene will pursue global clinical development

#### Terms

- HUTCHMED granted Inmagene four exclusive options (one per candidate) solely for the treatment of immunological diseases
- Option gives right to further develop, manufacture and commercialize that specific candidate worldwide
- HUTCHMED retains first right to co-commercialization in China
- Development milestones of up to US\$95 million
- Commercial milestones of up to US\$135 million
- Up to double-digit royalties



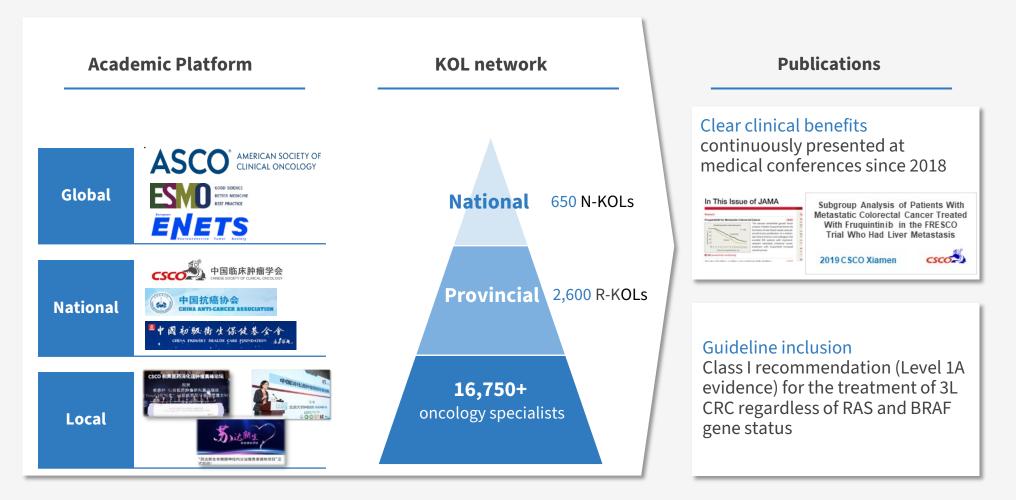


### COMMERCIALIZATION

### **KOL Relationships**



#### Good relationships with KOLs in major academic associations, covering solid & hematological cancers



### Guidelines for the Diagnosis and Treatment of HUTCHMED Pancreatic Neuroendocrine Tumors in China (2020)



(三) 靶向治疗

pNET 的靶向治疗主要包括依维莫司(mTOR抑制剂)、舒尼替尼(酪氨酸激酶抑制剂)和 索凡替尼(酪氨酸激酶抑制剂)。依维莫司适用于中、低级别的进展期pNET患者,其在抑 制肿瘤生长、延长患者中位无进展生存期方面具有明确价值(1A, I级推荐)[142]。 但依维莫司联合 SSA 可能无法进一步改善患者的远期预后[143],且其在化疗、PRRT 等失败的患者中可能引起更高的严重不良反应发生率[144]。舒尼替尼通常适用于分化较 好的进展期pNET 患者,其能抑制肿瘤生长并延长患者的无进展生存期(1A, I级推荐) [145]。但对于亚洲人群,标准剂量(37.5 mg/d)的舒尼替尼常引起较严重的不良反 应,而适当降低药物剂量(25 mg/d)并不影响舒尼替尼的临床有效性[146]。索凡替 尼同样适用于分化较好的进展期 pNET,其能延长患者的无病生存期,有望成为进展期 pNET 患者新的治疗选择(1A, I级推荐)[147]。 **"Surufatinib** is also suitable for well-differentiated advanced pNET, which can prolong disease-free survival in patients with advanced pNET and is expected to be a new treatment option for patients with advanced pNET (**1A, grade I recommendation**)."

### **Relationships with Patient Advocacy Groups**

#### >2,000 mCRC pts benefited from fruquintinib PAP program; surufatinib program recently initiated



#### Fruquintinib PAP program

✓ A successful program:

more than 2,000 mCRC patients benefited

- ✓ Close collaboration: with China Primary Health Care Foundation (Jan. 2019 - Aug. 2020)
- ✓ Donation management: incl. label, tax, free goods management, etc.

#### Surufatinib PAP program

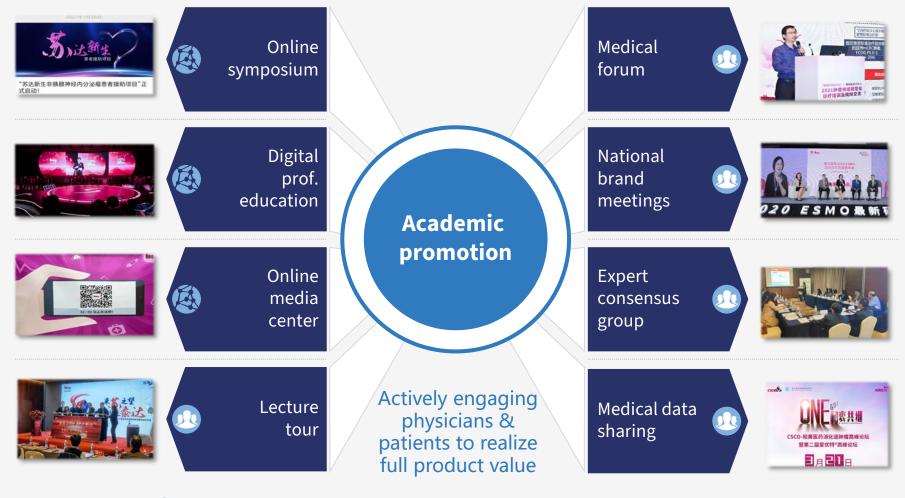
HUTCH

- ✓ Recently initiated with commercial launch
- ✓ Significant benefit for China NET patients expected given long survival period

### **Academic Promotion**



### Diversified Academic Promotion platforms to deliver product value to stakeholders









# **A5**

### MANUFACTURING EXPERTISE

### Manufacturing strategy



#### Some we control, some we outsource

	Small Molecule Manufacturing	Large Molecule Manufacturing
	Global Manufacturing/ formulation (Suzhou / Shanghai)	Collaborate with CDMOs
	<ul> <li>Formulation supported by HUTCHMED Suzhou (≤\$500m revenue)</li> </ul>	<ul> <li>2020-22: outsource mAb manufacturing to CDMOs.</li> </ul>
Formulation	<ul> <li>Long-term formulation (\$0.5-\$2.5bn revenue) incl. China &amp; global product supply → HUTCHMED Shanghai new factory</li> <li>Established ≤\$0.5bn capacity Suzhou 2018, now at steady</li> </ul>	<ul> <li>In parallel, establish own small scale lab mftg facilities to support discovery.</li> </ul>
	state; ~\$2.0bn capacity new Shanghai factory by 2024	<ul> <li>Build scale-up mAb mftg facilities in Shanghai new factory as</li> </ul>
	Global API Manufacturing	necessary.
	• Continue <b>to</b> outsource API unless we determine IP risk.	Establish CDMO collaboration during 2020 – in mid- to long-term
ΑΡΙ	Established Multiple 3 <sup>rd</sup> -party China-based API manufacturers have been established in past 10 years.	we will establish in-house mAb production.

### **CMC Development & Manufacturing**



#### Leadership



#### **Zhenping Wu, SVP**

- 13 years with HUTCHMED
- 30 years in pharma manufacturing including Roche and Pfizer



Process Research & Development

- 9 years with HUTCHMED
- 18 years in pharma manufacturing including Apotex and ChemPartner



Analytical Research & Development

- 8 years with HUTCHMED
- 25 years in pharma manufacturing including Merck and Sundia



- Drug Product Manufacturing & Supply Chain
- 11 years with HUTCHMED
- 20 years in pharma manufacturing including Bright Future and Frontage



- **Biologics CMC**
- 1 year with HUTCHMED
- 9 years in pharma manufacturing including Pfizer

- API process development
- Solid form selection
- Clinical material manufacturing
- Commercial API supplies

- Analytical method development
- API & drug product stability
- Commercial specification
- Regulatory CMC

- Formulation development
- Clinical supplies
- Commercial supplies
- Supply chain management

- Biological process development
- Biological formulation
- Biological method development
- Clinical supplies

### **Outsourcing API manufacturing**

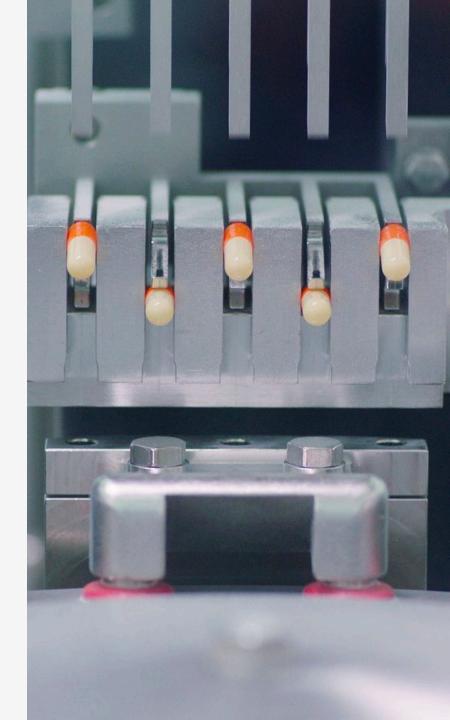
Advancing clinical pipeline and produce commercial supplies

• Work with leading CMOs in China for API manufacturing



### 

- Established strong relationships with CMOs from clinical manufacturing through commercialization
- Plan to have two sites qualified for each product for commercial manufacturing to mitigate supply risks



### **Drug Product and Biological Facilities**

New Shanghai Ea



New Shanghai factory to support production for China and global post 2025

#### **SUZHOU FACTORY**

- Built to produce ELUNATE<sup>®</sup> and SULANDA<sup>®</sup>
- Manufacturing talent developed
- Suzhou is designed to U.S. GMP standards

#### **SHANGHAI FACTORY**

- Capex of \$130 million over 5 years
- Will fulfil additional global production requirements
- Additional capacity for expansion in large molecule production



Ney Aspects	Suzhoù Factory	New Shanghar actory	
Property Type	Leased	Owned	
Land Size (sq.m.)	~1,800	~28,700 (16x)	
Building Size (sq.m.)	~4,500 (Office: ~1,000)	~55,000 (12x) (Office: ~16,400)	
Capacity (Cap & Tabs)	50 million	250 million (5x, Phase 1)	ļ
Growth Potential	No capacity for growth	Phase 2 for biologics	4







### **A6**

# FURTHER CORPORATE INFORMATION

### **Group Structure**

lttetje

### Main Entities / Offices

HUTCHMED

HUTCHMED Group Level (Nasdaq/AIM: HCM; HKEX:13)

### Oncology/Immunology

Discovery, development, manufacturing & commercialization of novel oncology & immunology therapeutics

Shanghai	New Jersey	Suzhou	Beijing
Discovery and	Clinical development	GMP-certified	Australia
development	& regulatory affairs	manufacturing	E.U.
Commercial			Others



Consolidated

Non-Consolidated

Other Ventures<sup>[1]</sup>

Hutchison Sinopharm Rx Commercialization Partner: Sinopharm Group (HCM 51%)

Shanghai Hutchison Pharmaceuticals Rx Mfg & Commercialization Partner: Shanghai Pharma (HCM: 50%)

 Not shown: Consumer Healthcare businesses, mainly 50/50 JV Hutchison Hain Organic and non-consolidated OTC 50/50 JV Hutchison Baiyunshan. Subject to regulatory approval, on Mar 24, 2021, agreement was signed to divest OTC JV.

### **Our Other Ventures have substantial value**



- HUTCHMED's Other Ventures continue to perform well relative to our peer group.
- Market value of our share of these JVs, based on China Pharma median PE multiples, approximately \$0.9 billion.<sup>[1]</sup>
- March 2021: agreed to divest smaller JV (OTC) for ~\$169m cash (~22x 2020 adjusted earnings to HUTCHMED of \$7.7m).<sup>[2]</sup>

			NET SALES			NET IN	СОМЕ		VALUATION	[4]
(US\$ millions)	Code	<b>2019</b> Jan-Jun	<b>2020</b> Jan-Jun	<b>19-20</b> Growth	<b>2019</b> Jan-Jun	<b>2020</b> Jan-Jun	<b>19-20</b> Growth	<b>2020</b> Margin	Market Cap.	P/E
HUTCHMED Other Ventures Subsidiaries/JVs <sup>[3]</sup>		367.1	365.2	-1%	57.0	62.4	9%	17%	n/a	n/a
Livzon Pharma	000513	705.6	727.9	3%	119.2	190.1	59%	26%	4,545	23
CR Double-Crane Pharma	600062	695.1	592.4	-15%	92.3	80.1	-13%	14%	1,726	12
Kunming Pharma	600422	536.6	489.2	-9%	34.4	32.4	-6%	7%	914	15
Zhejiang Pharma	600216	512.2	504.1	-2%	38.6	58.3	51%	12%	2,103	28
Tianjin Zhong Xin Pharma	600329	504.8	470.1	-7%	50.6	47.7	-6%	10%	1,624	21
Zhejiang Hua Hai Pharma	600521	379.0	472.2	25%	50.2	86.7	73%	18%	5,590	40
Shandong Xin Hua Pharma	000756	446.1	469.4	5%	23.4	26.9	15%	6%	666	17
Jiangsu Kang Yuan	600557	323.2	221.0	-32%	35.1	21.3	-39%	10%	855	19
Zhuzhou Qian Jin Pharma	600479	241.7	240.5	0%	14.8	13.6	-8%	6%	523	19
Jiu Zhi Tang	000989	241.2	261.9	9%	25.0	27.9	12%	11%	1,017	29
Peer Group Median (10 Comps. excl. HUTCHMED)		475.5	471.1	-1%	36.8	40.1	9%	9%	1,321	20

Peer Group: 10 companies (excl. HUTCHMED) selected are ALL listed and profitable mainland Chinese OTC/Rx pharma manufacturing companies, with a focus on similar product types, and 2020 Jan-Jun Net Sales in the ~\$200-750 million range.

Source: Company data, CICC.

[1] Peer group/China Pharma multiple of 20x 2020 actual Net income after tax of \$90.2m, excluding one-time land compensation; [2] HBYS' adjusted net profit attributable to HUTCHMED equity holders (after 20% non-controlling interest) in 2020 of \$7.7 million is a non-GAAP measure which is 40% of HBYS' 2020 net profit of \$91.3 million less \$72.0 million gain on land compensation, net of tax; [3] Total aggregate PRC domestic results of HUTCHMED's 6 Other Ventures companies (HBYS, SHPL, Hutchison Sinopharm, HHO, HHL & HCPL); [4] Market Capitalization and Price Earnings Ratios as at February 19, 2021: Trailing Twelve Month PE weighted averaged based on market capitalization.

### Non-GAAP Financial Measures & Reconciliation HUTCHMED

#### Other Ventures - Reconciliation of Non-GAAP Sales and Non-GAAP Net (Loss)/Income After Tax<sup>[1]</sup>

- Consolidated Subsidiaries: includes Hutchison Sinopharm and others
- Non-consolidated joint venture: includes SHPL and HBYS

					IFF	RS									US G	AAP					H1'20- H1'21
(US\$ millions)	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	H1'20	H1'21	Growth
Revenues (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	278.6	360.7	402.3	465.4	518.9	627.4	677.2	664.4	665.6	706.6	365.2	448.6	<b>23</b> %
Consolidated subsidiaries	4.7	6.1	9.3	8.9	3.7	5.5	7.0	14.1	14.9	15.5	16.5	67.0	126.2	180.9	205.2	172.9	178.1	197.8	90.4	114.5	27%
Non-consolidated joint venture	17.2	21.8	55.8	92.5	115.3	150.3	190.0	222.3	263.7	345.2	385.8	398.4	392.7	446.5	472.0	491.5	487.5	508.8	274.8	334.1	22%
Total Revenues Growth	n/a	27%	133%	<b>56</b> %	17%	31%	<b>26</b> %	<b>20</b> %	18%	<b>29</b> %	n/a	<b>16</b> %	11%	<b>21%</b>	8%	-2%	0%	<b>6</b> %		23%	
- GuanBao divested in Sept'2017	-	-	-	-	-	-	-	-	(11.4)	(50.5)	(51.6)	(49.7)	(40.7)	(45.0)	(38.6)	-	-	-	-	-	n/a
Adjusted Non-consolidated joint venture	17.2	21.8	55.8	92.5	115.3	150.3	190.0	222.3	252.3	294.7	334.2	348.7	352.0	401.5	433.4	491.5	487.5	508.8	274.8	334.1	22%
Adjusted Revenues (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	267.2	310.2	350.7	415.7	478.2	582.4	638.6	664.4	665.6	706.6	365.2	448.6	23%
Total Adjusted Revenues Growth	n/a	27%	133%	<b>56</b> %	17%	<b>31%</b>	<b>26</b> %	<b>20</b> %	<b>13</b> %	<b>16</b> %	13%	<b>19</b> %	15%	22%	<b>10%</b>	4%	0%	<b>6</b> %		23%	
Net (loss)/Income after tax (Non-GAAP)	(10.7)	(3.6)	2.2	6.7	11.2	14.7	21.5	27.9	30.1	33.1	39.7	48.8	54.1	63.3 <sup>[</sup>	<sup>3]</sup> 77.3 <sup>[·</sup>	<sup>4]</sup> 83.6	84.9	90.2 <sup>[</sup>	<sup>5]</sup> 62.4	73.3	<sup>[6]</sup> 17%
Consolidated subsidiaries	(10.3)	(4.9)	(2.9)	(2.4)	0.2	-	0.8	1.0	(0.4)	(1.1)	0.1	1.6	1.4	3.1	5.9	6.9	3.8	3.9	1.8	1.5	-20%
Non-consolidated joint venture	(0.4)	1.3	5.1	9.1	11.0	14.7	20.7	26.9	30.5	34.2	39.6	47.2	52.7	60.2	71.4	76.7	81.1	86.3	60.6	71.8	18%
Net (loss)/income attrib. to HUTCHMED	(5.7)	(3.7)	(0.5)	1.2	4.5	<sup>[2]</sup> 5.9 <sup>[</sup>	<sup>2]</sup> 9.3 <sup>[</sup>	<sup>2]</sup> <b>12.6</b>	<sup>[2]</sup> <b>13.6</b>	<sup>[2]</sup> <b>14.6</b> <sup>[</sup>	<sup>2]</sup> <b>18.2</b> <sup>[</sup>	<sup>2]</sup> <b>22.8</b> <sup>[</sup>	<sup>2]</sup> <b>25.2</b> <sup>[</sup>	<sup>2]</sup> <b>29.9</b> <sup>[</sup>	<sup>3]</sup> 37.5 <sup>[·</sup>	<sup>4]</sup> <b>41.4</b>	41.5	<b>44.0</b>	<sup>5]</sup> <b>30.4</b>	35.7	<sup>[6]</sup> 17%
Consolidated subsidiaries	(5.5)	(4.3)	(2.7)	(2.4)	0.2	0.0	0.8	1.0	0.0	(0.7)	0.2	1.3	1.0	1.8	3.9	4.8	2.9	2.8	1.4	1.2	-15%
Non-consolidated joint venture	(0.2)	0.6	2.2	3.6	4.3	5.9	8.5	11.6	13.6	15.3	18.0	21.5	24.2	28.1	33.6	36.6	38.6	41.2	29.0	34.5	19%
Net (loss)/income attrib. to HUTCHMED growth	n/a	-35%	-86%	340%	275%	31%	58%	35%	8%	7%	n/a	26%	10%	19%	25%	10%	0%	6%		17%	

[1] 2003–2006 incl. disco. operation; [2] Continuing Operations; [3] Excludes the land compensation in SHPL of \$80.8 million from net income after tax and \$40.4 million from net income attributable to HUTCHMED for 2016;

[4] Excludes SHPL's R&D related subsidies of \$5.0 million from net income after tax and \$2.5 million from net income attributable to HUTCHMED for 2017;

[5] Excluded the land compensation in HBYS of \$72.0 million from net income after tax and \$28.8 million from net income attributable to HUTCHMED for 2020.

[6] Excluded the land compensation in HBYS of \$14.1 million from net income after tax and \$5.6 million from net income attributable to HUTCHMED for H1 2021.



### July'17 – 15 new drugs in oncology<sup>[1]</sup> added to NRDL

		Ur	nit Pricing (l	JS\$) <sup>[3]</sup>		Approximate Mon	thly Pricing	; (US\$) <sup>[3]</sup>	
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	Indication coverage
Herceptin <sup>®</sup> (trastuzumab)	Roche	440mg:20ml	\$3,298.81	\$1,125.93	-66%	Breast: 4mg/kg wk 1, 2mg/kg weekly	\$4,500	\$1,540	Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
Avastin® (bevacizumab)	Roche	100mg:4ml	\$772.74	\$296.00	-62%	10mg/kg Q2W	\$11,590	\$4,440	Late-stage meta. CRC or advanced non-squamous NSCLC.
TheraCIM <sup>® [4]</sup> (nimotuzumab)	Biotech Pharma	50mg:10ml	\$435.26	\$251.85	-42%	100mg weekly	\$3,730	\$2,160	Combo with radiotherapy for EGFR+ Stage III/IV nasopharyngeal carcinoma.
Rituxan® (rituximab)	Roche	500mg:50ml <sup>[2]</sup>	\$2,544.74	\$1,228.15	-52%	375 mg/m² weekly	\$13,090	\$6,320	Restorative or resistant follicular central type lym.; CD20+ stage III-IV follicular NHL, CD20+ DLBCL.
Tarceva® (erlotinib)	Roche	150mg <sup>[2]</sup>	\$68.15	\$28.89	-58%	150mg QD	\$2,040	\$870	Advanced NSCLC with limited EGFR gene mutation.
Nexavar® (sorafenib)	Bayer	0.2g	\$60.44	\$30.07	-50%	400mg BID	\$7,250	\$3,610	Unresectable RCC. Unresectable HCC. Meta. Diff. thyroid after radio-iodine therapy.
Tykerb® (lapatinib)	GSK	250mg	\$17.63	\$10.37	-41%	1,500mg QD	\$3,170	\$1,870	Adv./meta. breast cancer with Her2 O/E, after anthracycline, paclitaxel, trastuzumab.
AiTan® (apatinib)	Hengrui	425mg <sup>[2]</sup>	\$47.85	\$30.22	-37%	850mg QD	\$2,870	\$1,810	3L gastric adenocarcinoma or esophageal junction with adenocarcinoma.
Velcade® (bortezomib)	1&1	3.5mg <sup>[2]</sup>	\$1,873.78	\$906.07	-52%	1.3mg/m <sup>2</sup> quartic every 3 wks	\$6,360	\$3,080	Myeloma; recurring or refractory mantle cell lymphoma.
EnDu® (rh-endostatin)	Simcere	15mg	\$132.15	\$93.33	-29%	7.5mg/m <sup>2</sup> iv QD, 2-wks-on / 1-week-off	\$2,110	\$1,490	Late-stage NSCLC.
Epidaza® (chidamide)	Chipscreen	5mg	\$81.48	\$57.04	-30%	30mg QD, 2x per wk	\$4,190	\$2,930	2L+ Recurring or refractory peripheral T-cell lymphoma (PTCL).
Zytiga® (abiraterone)	J&J	250mg	\$45.63	\$21.48	-53%	1,000mg QD	\$5,480	\$2,580	Metastatic or ovariectomized prostate cancer.
Faslodex® (fulvestrant)	AstraZeneca	250mg:5ml	\$806.81	\$355.56	-56%	500mg per month	\$1,610	\$710	Advanced ER/PR+ breast can., failing aromatase inhibitor.
Afinitor® (everolimus)	Novartis	5mg <sup>[2]</sup>	\$36.44	\$21.93	-40%	10mg QD	\$2,190	\$1,320	Adv. RCC after sunitinib or sorafenib. Adv./meta. pancreatic NETs. Tuberous sclerosis with renal angiomyolipoma.
Revlimid (lenalidomide)	Celgene	25mg <sup>[2]</sup>	\$413.93	\$163.26	-61%	25mg QD, 3-wks-on / 1-wk-off	\$9,310	\$3,670	2L+ Recurring myeloma.

Source: Ministry of Human Resources and Social Security (MOHRSS); Yaozhi; BofA Merrill Lynch Global Research.

[1] Excluding 3 botanical oncology drugs; [2] Reference SKU or reference recommended dosage for monthly pricing calculation; [3] Calculation assumes an exchange rate of CN¥6.75 per US\$1; [4] Marketed as Tai Xin Sheng® in China.



### Oct'18 – 17 new drugs in oncology added to NRDL

			Unit Prici	ng (US\$) <sup>[2]</sup>		Approximate Monthly P	ricing (US\$)	[2]	
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	Δ%	Dosage <sup>[1]</sup>	Avg. Tender	Reimbursed	Indication coverage
Focus V® (anlotinib)	Sino Biopharm	12mg	\$127	\$70	-45%	12mg QD (2 wks-on/1-wk-off)	\$2,500	\$1,417	3L NSCLC
Oncaspar <sup>®</sup> (pegaspargase)	Hengrui	5ml: 3750 IU	\$560	\$429	-23%	≤2ml every 14 days	\$1,231	\$943	1L ALL
Vidaza® (azacitidine)	Celgene	100mg	\$378	\$152	-60%	1 <sup>st</sup> cycle: 75mg QD for 7 days; 4wk cycle. After 2 cycles increase dose to 100mg, min of 4-6 cycles	\$14,022	\$5,636	Refractory anemia (RA) or RA with ringed sideroblasts (RARS), RA with excess blasts (RAEB / RAEB-T), and chronic myelomonocytic leukemia (CMMoL)
Inlyta® (axitinib)	Pfizer	5mg	\$99	\$30	-70%	5mg BID	\$5,957	\$1,787	2L advanced renal cell carcinoma
Tagrisso <sup>®</sup> (osimertinib)	AstraZeneca	80mg	\$253	\$73	-71%	80mg QD	\$7,597	\$2,201	EGFR TKI refractory T790M+ NSCLC
Ninlaro® (ixazomib)	Takeda	4mg	\$3,234	\$710	-78%	4mg on Days 1, 8, 15 (28 day cycle)	\$12,934	\$2,839	2L multiple myeloma
Xalkori® (crizotinib)	Pfizer	250mg	\$123	\$37	-70%	250mg BID	\$7,407	\$2,245	Locally adv. or meta. ALK+ or ROS1+ NSCLC
Gilotrif® (afatinib)	Boehringer	40mg	\$116	\$29	-75%	40mg QD	\$3,483	\$863	NSCLC with EGFR
Tasigna® (nilotinib)	Novartis	200mg	\$39	\$14	-65%	400mg BID	\$4,645	\$1,635	CML
Votrient <sup>®</sup> (pazopanib)	Novartis	200mg	\$66	\$23	-65%	800mg QD	\$7,891	\$2,348	RCC
Sutent® (sunitinib)	Pfizer	12.5mg	\$49	\$22	-55%	GIST & RCC: 50mg QD pNET: 37.5mg QD	\$5,544 \$4,455	\$2,498 \$2,007	RCC, GIST, pNET
Stivarga® (regorafenib)	Bayer	40mg	\$52	\$28	-46%	160mg QD, 3-wks-on/1-wk-off *	\$4,368	\$2,352	Meta. CRC, GIST, HCC
Zykadia® (ceritinib)	Novartis	150mg	\$108	\$28	-74%	450mg QD	\$9,699	\$2,564	ALK+ adv. or meta. NSCLC
Zelboraf® (vemurafenib)	Roche	240mg	\$30	\$16	-47%	960mg BID	\$7,252	\$2,369	Melanoma
Erbitux® (cetuximab)	Merck	100mg	\$571	\$186	-67%	400mg/m2 initial dose, 250mg weekly	\$10,446	\$3,074	Colorectal cancer, head and neck cancer
Sandostatin LAR® (octreotide)	Novartis	20mg	\$1,169	\$835	-29%	20mg Q4W	\$1,169	\$835	GEP-NENs
Imbruvica® (ibrutinib)	JNJ	140mg	\$78	\$27	-65%	MCL: 560mg QD CLL & WM: 420mg QD	\$9,324 \$6,993	\$3,263 \$2,447	MCL, CLL/SLL

Source: Ministry of Human Resources and Social Security (MOHRSS); Yaozhi; China Merchants Securities Research; Citi Global Research; Frost & Sullivan. [1] Reference SKU or reference recommended dosage for monthly pricing calculation; [2] Calculation assumes an exchange rate of CN¥6.95 per US\$1. \* Price amended to account for 3-weeks on, 1 week off regimen.



#### Nov'19 update – 8 new drugs in oncology<sup>[1]</sup>

			Unit Pricin	ng (US\$) <sup>[2]</sup>		Approximate Monthly	y Pricing (U	S\$) <sup>[2]</sup>	
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	Indication coverage
Elunate® (fruquintinib)	HUTCHMED	5mg	\$161	\$58	-64%	5mg QD 3wks/1wk-off.	\$3,378	\$1,221	Metastatic colorectal cancer, 3L
Tyvyt® (sintilimab)	Innovent	10ml (100mg)	\$1,206	\$437	-64%	200mg Q3W	\$3,216	\$1,166	Classical Hodgkin's lymphoma, 3L
Saiweijian® (raltitrexed)	Sino Biopharm	2mg	\$232	\$103	-56%	3mg/m <sup>2</sup> Q3W	\$765	\$340	Colorectal cancer, 5-FU intolerable
Alecensa® (alectinib)	Roche	150mg	\$32	\$10	-70%	600mg, BID	\$7,689	\$2,343	NSCLC, ALK+
Lynparza® (olaparib)	AstraZeneca	150mg	\$68	\$26	-62%	300mg, BID	\$8,173	\$3,120	Epithelial ovarian, fallopian tube, or peritoneal cancer
Airuini® (pyrotinib)	Hengrui	80mg	\$39	\$13	-66%	400mg QD, 21 days	\$4,118	\$1,389	Breast cancer, HER2+, 2L
Perjeta® (pertuzumab)	Roche	420mg	\$2,892	\$762	-74%	840mg wk1, 420mg Q3W	\$8,676	\$2,286	Breast cancer, HER2+, neoadjuvant
Jakafi® (ruxolitinib)	lncyte / Novartis	5mg	\$20	\$9	-56%	Dose is based on patient's baseline platelet count: • (a) >200 X 10 <sup>9</sup> /L: 20 mg BID • (b) 100 X 10 <sup>9</sup> /L: 200 X 10 <sup>9</sup> /L: 15 mg BID • (c) 50 X 10 <sup>9</sup> /L to 100 X 10 <sup>9</sup> /L: 5 mg given BID	(a) \$4,800 (b) \$3,600 (c) \$1,200	(a) \$2,160 (b) \$1,620 (c) \$540	PMF, PPV-MF, PET-MF

Source: National Healthcare Security Administration (NHSA); Frost & Sullivan.

[1] Excluding botanical oncology drugs; [2] Calculation assumes an exchange rate of CN¥6.5 per US\$1.



#### Nov'19 update – 9 renewed drugs in oncology<sup>[1]</sup>

			Unit Pricing (	US\$) <sup>[2]</sup>		Approximate Monthl	y Pricing (US	\$) [2]	
Brand (generic)	Company	Dosage	'17 NRDL	'19 NRDL	Δ%	Dosage	'17 NRDL	'19 NRDL	Indication coverage
AiTan® (apatinib)	Hengrui	425mg <sup>[3]</sup>	\$30	\$27	-13%	850mg QD	\$1,823	\$1,594	3L gastric adenocarcinoma or GEJ with adenocarcinoma.
EnDu® (rh-endostatin)	Simcere	15mg	\$97	\$75	-22%	7.5mg/m <sup>2</sup> iv QD, 2wks/1wk-off	\$1,681	\$1,308	Late-stage NSCLC.
Epidaza® (chidamide)	Chipscreen	5mg	\$53	\$59	-11%	30mg QD, 2x per wk	\$2,843	\$2,533	2L+ Recurring or refractory peripheral T-cell lymph. (PTCL).
Herceptin® (trastuzumab)	Roche	440mg	\$1,169	\$846	-28%	3wks regimen: 8mg/kg wk1, 6mg/kg Q3W	\$1,276	\$923	Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
Avastin® (bevacizumab)	Roche	100mg	\$307	\$231	-25%	3wks regimen: CRC: 7.5mg/kg Q3W NSCLC: 15mg/kg Q3W	CRC: \$1,844 NSCLC: \$3,689	CRC: \$1,385 NSCLC: \$2,769	Late-stage meta. CRC or advanced non-squamous NSCLC.
TheraCIM <sup>® [4]</sup> (nimotuzumab)	Biotech	50mg	\$262	\$221	-16%	100mg, QW	\$2,092	\$1,766	Combo with RT for EGFR+ III/IV nasopharyngeal carcinoma.
Tarceva® (erlotinib)	Roche	150mg	\$28	\$12	-56%	150mg, QD	\$841	\$374	Advanced NSCLC with limited EGFR gene mutation.
Nexavar® (sorafenib)	Bayer	200g	\$29	\$14	-53%	400g BID	\$3,519	\$1,662	RCC or HCC. meta. diff. thyroid after radio-iodine therapy.
Afinitor® (everolimus)	Novartis	5mg	\$23	\$20	-12%	RCC: 10mg, QD Pan-NETs: 10mg, QD	\$1,366	\$1,200	RCC after sunitinib or sorafenib. Pancreatic NETs. TSRA.

Source: National Healthcare Security Administration (NHSA); Frost & Sullivan.

[1] Excluding botanical oncology drugs; [2] Calculation assumes an exchange rate of CN¥6.5 per US\$1; [3] Reference SKU or reference recommended dosage for monthly pricing calculation; [4] Marketed as Tai Xin Sheng® in China.



### Dec'20 update – 13 new oncology drugs through negotiation<sup>[1]</sup>

			Unit Pricin	g (US\$) <sup>[2]</sup>		Approximate Mor	thly Pricing	(US\$) <sup>[2]</sup>		
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	Indication coverage	
Lipusu <sup>®</sup> (paclitaxel liposome)	Luye Pharma	30mg	\$129	\$35	-73%	155mg/m <sup>2</sup> Q3W	\$1,470	\$399	1L+ metastatic ovarian cancer, breast cancer, 1L NSCLC	
Ciptertin <sup>®</sup> (inetetamab)	3SBio	50mg	\$235	\$91	-61%	initial 4mg/kg, maintenance 2mg/kg	\$2,260	\$871	HER2+ metastatic breast cancer	
Baizean® (tislelizumab)	BeiGene	100mg	\$1,644	\$335	-80%	200mg Q3W	\$4,385	\$894	3L relapsed or refractory classical Hodgkin's lymphoma, locally adv. or meta. urothelial cancer	
Tuoyi <sup>®</sup> (toripalimab)	Junshi Biosciences	240mg	\$1,108	\$323	-71%	3mg/kg Q2W	\$1,662	\$485	Non-excisional or metastatic melanoma	
AiRuiKa® (camrelizumab)	Hengrui	200mg	\$3,046	\$450	-85%	cHL&EC: 200mg Q2W NSCLC: 200mg Q3W HCC: 33mg/kg Q3W	\$6,092 \$4,062 \$40,209	\$601	3L relapsed or refractory classical Hodgkin's lymphoma, advanced HCC, 1L locally adv. or meta. non-squamous NSCLC, esophageal cancer	
Xinfu® (flumatinib)	Hansoh Pharma	200g	\$27	\$10	-63%	600mg QD	\$2,430	\$900	Ph+ chronic myelogenous leukemia	
Ameile® (almonertinib)	Hansoh Pharma	55mg	\$75	\$27	-64%	110mg QD	\$4,523	\$1,625	EGFR TKI refractory T790M+ locally advanced or metastatic NSCLC	
Brukinsa® (zanubrutinib)	BeiGene	80mg	\$27	\$15	-44%	320mg QD	\$3,260	\$1,828	2L MCL, 2L CLL / SLL	
Mekinist <sup>®</sup> (trametinib)	Novartis	2mg	\$142	\$57	-60%	2mg QD	\$4,254	\$1,705	BRAF V600M+ non-excisional or metastatic melanoma	
Tafinlar® (dabrafenib)	Novartis	75mg	\$53	\$14	-74%	150mg BID	\$6,380	\$1,705	BRAF V600M+ non-excisional or metastatic melanoma	
Lenvima <sup>®</sup> (lenvatinib)	Eisai	4mg	\$86	\$17	-81%	12mg QD	\$7,754	\$1,495	HCC	
Xtandi® (enzalutamide)	Astellas Pharma	40mg	\$49	\$11	-78%	160mg QD	\$5,880	\$1,285	Castration-resistant prostate cancer (CRPC)	
Zejula® (niraparib)	Zai Lab	100mg	\$128	\$31	-76%	300mg QD	\$11,534	\$2,769	Relapsed epithelial ovarian, fallopian tube or primary peritoneal carcinoma	

Source: National Healthcare Security Administration (NHSA); Frost & Sullivan.

[1] Excluding traditional Chinese medicines; [2] Calculation assumes an exchange rate of CN¥6.5 per US\$1.



### Dec'20 update – 15 renewed drugs in oncology<sup>[1]</sup>

		Unit Pricing (US\$) <sup>[2]</sup>				Approximate Monthly Pricing (US\$) <sup>[2]</sup>			
Brand (generic)	Company	Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	Indication coverage
Focus V® (anlotinib)	Sino Biopharm	12mg	\$75	\$47	-37%	12mg QD (2 wks-on/1-wk-off)	\$1,515	\$952	3L NSCLC, 3L SCLC, STS
Oncaspar® (pegaspargase)	Hengrui	5ml: 3750 IU	\$584	\$458	-21%	≤2ml every 14 days	\$1,283	\$1,006	1L ALL
Inlyta® (axitinib)	Pfizer	5mg	\$32	Undisclosed	-	5mg BID	\$1,920	-	2L advanced renal cell carcinoma
Tagrisso® (osimertinib)	AstraZeneca	80mg	\$78	\$28	-64%	80mg QD	\$2,350	\$860	1L NSCLC harboring EGFR exon 19 deletions or exon 21 L858R mutations; EGFR TKI refractory T790M+ NSCLC
Ninlaro® (ixazomib)	Takeda	4mg	\$759	Undisclosed	-	4mg on Days 1, 8, 15 (28 day cycle)	\$2,277	-	2L multiple myeloma
Xalkori® (crizotinib)	Pfizer	250mg	\$40	\$35	-12%	250mg BID	\$2,400	\$2,112	Locally adv. or meta. ALK+ or ROS1+ NSCLC
Tasigna® (nilotinib)	Novartis	200mg	\$15	Undisclosed	-	400mg BID	\$1,800	-	CML
Votrient <sup>®</sup> (pazopanib)	Novartis	200mg	\$25	Undisclosed	-	800mg QD	\$2,510	-	RCC
Stivarga® (regorafenib)	Bayer	40mg	\$30	\$26	-12%	160mg QD, 3-wks-on/1-wk-off	\$2,520	\$2,217	Meta. CRC, GIST, HCC
Zykadia® (certinib)	Novartis	150mg	\$30	Undisclosed	-	450mg QD	\$2,700	-	ALK+ adv. or meta. NSCLC
Zelboraf® (vemurafenib)	Roche	240mg	\$17	Undisclosed	-	960mg BID	\$4,080	-	BRAF V600 Melanoma
Erbitux® (cetuximab)	Merck	100mg	\$199	Undisclosed	-	400mg/m <sup>2</sup> initial dose, 250mg QW	\$1,990	-	Colorectal cancer, head and neck cancer
Sandostatin LAR® (octreotide)	Novartis	20mg	\$892	Undisclosed	-	20mg Q4W	\$892	-	GEP-NENs
Imbruvica® (ibrutinib)	JNJ	140mg	\$29	Undisclosed	-	MCL: 560mg QD CLL & WM: 420mg QD	MCL: \$3,489 CLL&SLL: \$2,617	-	MCL, CLL/SLL, WM
Lynparza® (olaparib)	AstraZeneca	150mg	\$26	Undisclosed	-	300mg, BID	\$1,560	-	BRCAm epithelial ovarian, fallopian tube, or peritoneal cancer

Source: National Healthcare Security Administration (NHSA); Frost & Sullivan.

[1] Excluding traditional Chinese medicines; [2] Calculation assumes an exchange rate of CN¥6.5 per US\$1.