Wednesday, August 4, 2021

Company Report

China Merchants Securities (HK) Co., Ltd.
Hong Kong Equity Research

Hutchmed (HCM US)

Building momentum towards a fully-fledged biopharma

- **Hutchmed (HCM) is a China-based biopharma company with an proven in-house innovative pipeline focusing on oncology**
- **HCM extends its global commercial footprint, paving the way for internal pipeline monetization and external BD opportunities**
- **We initiated coverage on HCM with a BUY rating and FY22E SOTP-based TP of USD54.6, implying 28% upside potential**

R&D validated by broad portfolio / global collaborations

HCM has a capable in-house small molecule R&D platform that boasts superior selectivity and safety profile in its pipeline assets. HCM now has three commercial oncology drugs (fruquintinib, surufatinib, savolitinib) in China and one U.S. NDA/EMA MAA filed (surufatinib), proving its internal R&D capabilities. HCM's R&D platform is further validated by multiple global partnerships (AZ collaboration for savolitinib; various PD-1 combo studies for surufatinib and fruquintinib). In addition, we see promise for HCM's other early-stage candidates (i.e. HMPL-689, HMPL-523, HMPL-A83, etc.), which should continue to unlock value of its R&D pipeline.

Well-built commercial franchise to drive value accretion

We believe HCM's has established a commercial team of 540+ oncology-focused sales reps to support its efforts in innovative therapeutic development. The team has demonstrated strong capability to boost ELUNATE sales since HCM assumed commercial role in 4Q20 (HCM sales team achieved USD40.1mn in-market sales in 1Q 2021 vs. Eli Lilly's USD23.5mn in total over Q1-Q3 2020). Further, HCM is building up its U.S. sales team to support the potential launch of surufatinib in 2022E and fruquintinib in 2023E. We identify the enhancing global capability will add more strength to HCM's commercial franchise.

Major catalysts to watch in 1H21E/22E

1) **Surufatinib:** PD-1 combo readout in late '21E; U.S. NDA & E.U. MAA approval (NETs mono) in '22E; 2) **Fruquintinib:** PD-1 combo readout in late '21E; FRESCO-2 ph3 readout & NDA subm. (CRC) in ex-China in '22E; FRUTIGA ph2 readout & NDA subm. (GC) in China in '22E; 3) **HMPL-689 & HMPL 523**: data readout in late '21E.

We initiate with BUY, SOTP-based TP of USD54.6

Our SOTP-based TP mainly covers surufatinib (valued at ~USD2.4bn), fruquintinib (~USD1.0bn), savolitinib (~USD2.4bn), and nine early clinical-stage assets (~USD1.0bn in total). We estimate Co. to generate revenue of USD334mn/425mn/567mn in 2021-23E, but remain a loss position due to large R&D spending. For the HKEX share, we assume same methodology to arrive TP at HKD84.8/shr (1 ADR shr = 5 HKEX shrs, USD/HKD FX rate assumed at 7.77).

USD mn	2019	2020	2021E	2022E	2023E
Revenue	205	228	334	425	567
yoy growth	-4%	11%	47%	27%	34%
Adjusted net profit	(94)	(106)	(271)	(287)	(239)
yoy growth	n.a.	n.a.	n.a.	n.a.	n.a.

Sources: Company data, CMS (HK) estimates

Hayden Zhang, CFA
+852 3189 6354
haydenzhang@cmschina.com.hk

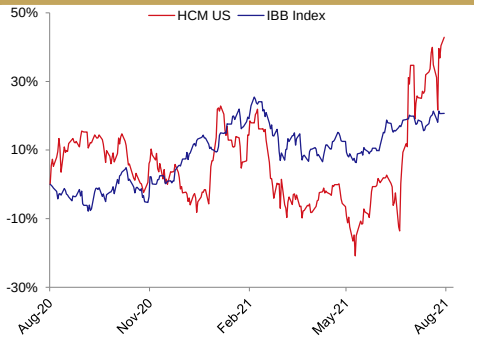
Warren Dai, CFA
+852 3189 6126
warrendai@cmschina.com.hk

Initiation

BUY

Price (August 2, 2021)	USD42.79
12-month Target Price (Potential up/downside)	USD54.6 (+28%)

Price Performance



Source: Bloomberg

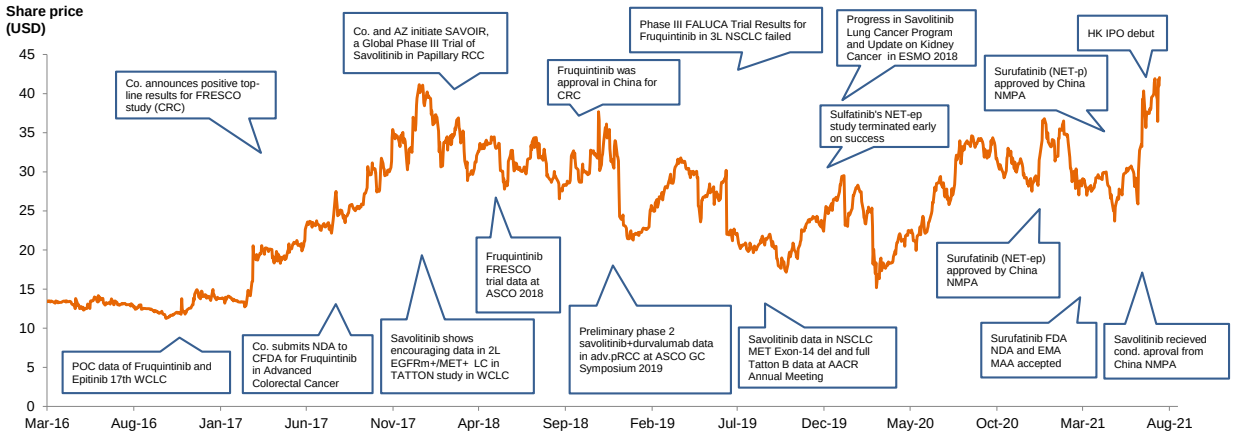
%	1m	6m	12m
HCM US	6.1	33.7	42.9
HSI	0.7	2.0	20.7

Pharmaceutical & Healthcare	
NASDAQ (August 2, 2021)	14,681
IBB (August 2, 2021)	166
Key Data	
52-week range (USD)	23.7-43.9
Market cap (USD mn)	7,395
Avg. daily traded value (USD mn)	15.1
BVPS (USD)	4.85
Shareholding Structure	
CK Hutchison	38.5%
Directors	2.1%
Free float	59.4%

Sources: Company data, Bloomberg

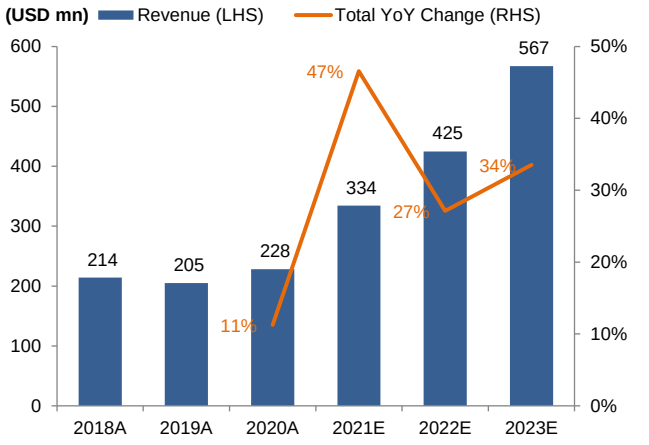
Focus charts

Figure 1: HCM's share price performance since 2016



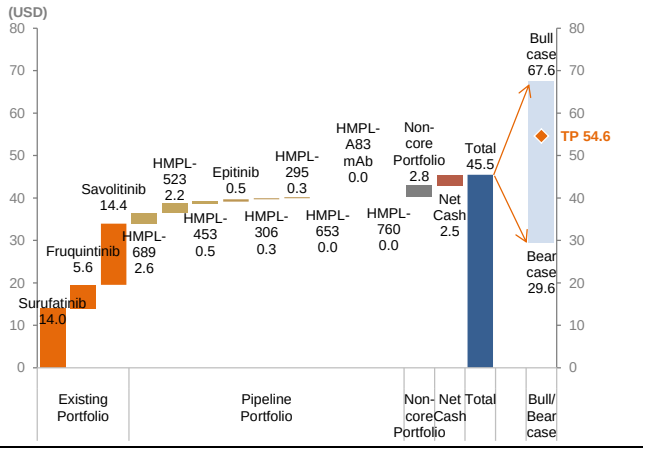
Sources: Bloomberg, CMS (HK)

Figure 2: Total revenue and growth during 2018-23E



Sources: Company data, CMS (HK) estimates

Figure 3: rNAV per share breakdown



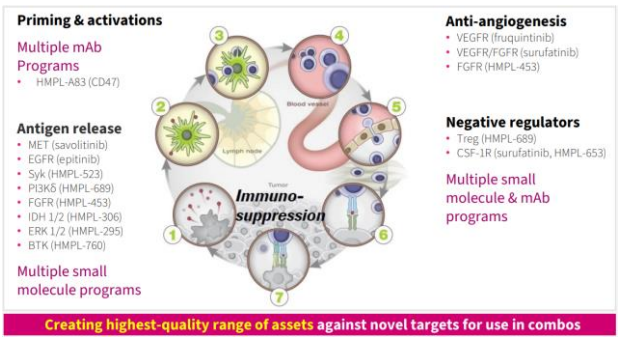
Sources: Company data, CMS (HK) estimates

Figure 4: Catalyst calendar

Candidates	Target	Indication	YE20/21-23E Milestone / Event	Timeline	Achievement
Savolitinib	c-MET	Exon-14m skipping NSCLC	NDA approval (CN)	Jun, 2021	√
		2L/3L EGFRm+ NSCLC	Topline data readout	1H22E	
Surufatinib	FGFR1/2/3 FGFR1 CSF-1R	NET (non-pacreatic)	NDA approval (CN)	Dec, 2020	√
			Product Launch (CN)	Jan, 2021	√
			NDA filing (US)	Apr, 2021	√
		NET (pacreatic)	NDA approval (CN)	Jun, 2021	√
			EMA MAA filing (EU)	Jun, 2021	√
			PADUFA date/launch (US)	1H22E	
Fruquintinib	FGFR1/2/3	2L GC	Topline data readout	2H22E	
		PD-1 combo	Ph2 data readout	YE21E	
HMPL-689	PI3Kδ	2L FL/MZL	Data readout (CN)	YE21E	
HMPL-523	Syk	ITP	Data readout (CN)	YE21E	

Sources: Company data, CMS (HK) estimates

Figure 5: Drug discovery platform



Sources: Company data, CMS (HK) estimates

Company background

Hutchmed (HCM, hereafter referred to as Company), founded in 2000, is a China-based biopharma company with an innovative platform comprising of a broad range of in-house developed small molecules focusing on molecular targeted therapy and immuno-oncology.

Company has a capable in-house small molecule discovery and development platform that boasts superior selectivity and safety profile in pipeline assets. Currently, the company has nine novel drug candidates in clinical development, of which three received market approval in China: 1) ELUNATE (fruquintinib, VEGFR1/2/3 inhibitor) was approved for the treatment of 3L colorectal cancer (mCRC), and 2) SULANDA (surufatinib, VEGFR 1/2/3, FGFR1 & CSF-1R) was approved for the treatment of pancreatic and non-pancreatic neuroendocrine tumors (ep/p-NET,) and has completed the NDA submission to the FDA in April 2021; and 3) Savolitinib (c-MET inhibitor) was approved for the treatment of NSCLC MET exon14 skipping.

HCM operates a collaborative research and marketing model partnering with several MNCs and established domestic players. It entered into collaboration agreements with AstraZeneca (AZN LN, NR) on Savolitinib and is entitled to receive up to USD120mn development milestone and several hundred million USD commercial milestone, with 14%-18% sales royalty outside China and 30% sale royalty in China. It also partnered with PD-1/L1 majors to explore the PD-1/L1 combination with its fruquintinib or surufatinib targeting varied tumor indications.

The below chart shows HCM's innovative drug pipeline.

Figure 6: Summary of HCM pipeline portfolio

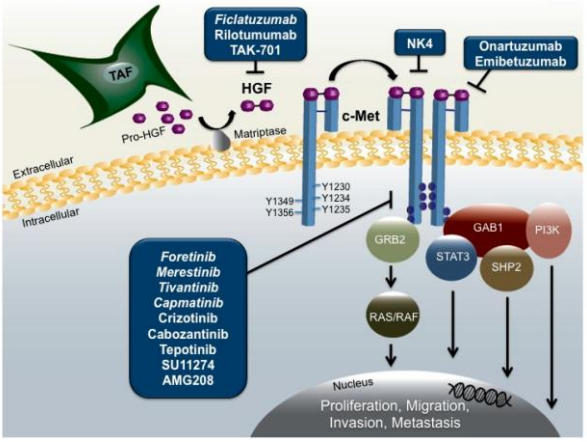
Product (Brand)	MoA	Indications	Partner	Rights	Lead Indication	
					China	Global
Savolitinib (ORPATHYS)	c-MET	NSCLC/RCC/ GC/CRC	AZ	Global: 9-18% China: 30%	**Marketed** (NSCLC) **Ph3** (GC, NSCLC combo)	**Ph2/3** (multiple NSCLC) **Ph3** (PRCC)
Frquintinib (ELUNATE)	VEGFR1/2/3	CRC/GC/ NSCLC/ST	Eli Lilly	Global: 100% China: 70-80%	**Marketed** (3L CRC) **Ph3** (GC)	**Ph3 U.S., E.U., Japan** (CRC)
Surufatinib (SULANDA)	VEGFR1/2/3 FGFR/CSF-1R	NET/BTC/ TC/ST	n.a.	WW right	**Marketed** (ep-NET/p-NET)	**U.S. NDA & E.U. MAA filings accepted** (NET)
HMPL-689	PI3Kδ	B-cell malig. (iNHL)	n.a.	WW right	**Ph2 reg-intent** (FL/MZL)	**Ph1 US/EU/AUS** (NHL)
HMPL-523	Syk	B-cell malig. (iNHL)/ITP	n.a.	WW right	**Ph1b/2** (NHL)	**Ph1 US/EU/AUS** (NHL)
HMPL-453	FGFR1/2/3	CCA	n.a.	WW right	**Ph2** (HCC)	n.a.
Epitinib	EGFRm+	GBM	n.a.	WW right	**Ph2** (GBM)	n.a.
HMPL-306	IDH1/2	Hemato malig. Solid tumor	n.a.	WW right	**Ph1** (Hemato malig.)	**Ph1** (Hemato malig./ Solid tumors)
HMPL-295	ERK (MAPK)	Solid tumor	n.a.	WW right	**Ph1** (Solid tumors)	n.a.
HMPL-760	3rd Gen BTK	Hemato malig.	n.a.	WW right	IND submitted June 2021	IND submitted June 2021
HMPL-653	CSF-1R	Solid tumor	n.a.	WW right	IND submission 2021E (US/China)	
HMPL-A83	CD47	Hemato malig. Solid tumor	n.a.	WW right	IND submission 2021E (US/China)	

Source: Company data; Note: LOE: loss of exclusivity, WW: worldwide, NSCLC: non-small lung cancer, RCC: renal cell carcinoma, GC: gastric cancer, CRC: colorectal cancer, NET: neuroendocrine tumor, ep/p: extra-pancreatic/pancreatic, BTC: biliary tract cancer, TC: thyroid cancer, ST: solid tumor; iNHL: indolent non-Hodgkin lymphoma, CCA: cholangiocarcinoma, GBM: glioblastoma; Hemato malig.: hematology malignancy

Savolitinib (c-MET inhibitor)

Savolitinib (out-licensed to AstraZeneca) is a c-mesenchymal-epithelial transition factor (c-MET or MET) inhibitor being investigated clinically in several solid tumors including NSCLC, GC, and RCC. MET signaling is important in cellular processes such as differentiation, proliferation, cell cycle motility and apoptosis. Dysregulation of MET signaling has been known to confer to EGFR acquired resistance in patients with NSCLC. While there are a number of multi-kinase inhibitors which target MET (e.g. Cabometyx, Xalkori) that have been approved to treat a variety of advanced solid tumors (RCC, NSCLC, etc.), there are currently only three approved selective MET inhibitors (capmatinib, tepotinib, savolitinib) with a number of competitive MET inhibitors in clinical development.

Figure 7: An illustration of the mechanisms of action of currently available c-MET/HGF receptor inhibitors



Sources: MDPI

MET activity can be dysregulated in several ways such as MET protein overexpression, MET gene amplification or MET gene mutations. Among them, MET protein overexpression is the most frequent, accounting for 25-75% of NSCLC patients. MET gene amplification is reported in 2-4% untreated NSCLC patients and 5-20% of patients with EGFR-mutated tumors and acquired resistance to EGFR TKIs. MET exon 14 deletions occur in approximately 3-4% of NSCLC cases. (Source: Giulia Pasquini, et al. Expert Opinion on Investigational Drugs. Vol 27, 2018). Consequently, researchers are exploring the use of MET inhibitor as a mono-therapy for NSCLC patients with MET dysregulation, as well as the concurrent use of both EGFR inhibitors and MET inhibitors for NSCLC patients with acquired EGFR resistance. In particular, the increasing use of Tagrisso (osimertinib) for 1st line treatment of patients with NSCLC (approved in April 2018) should dramatically increase the clinical need for efficacious MET inhibitors.

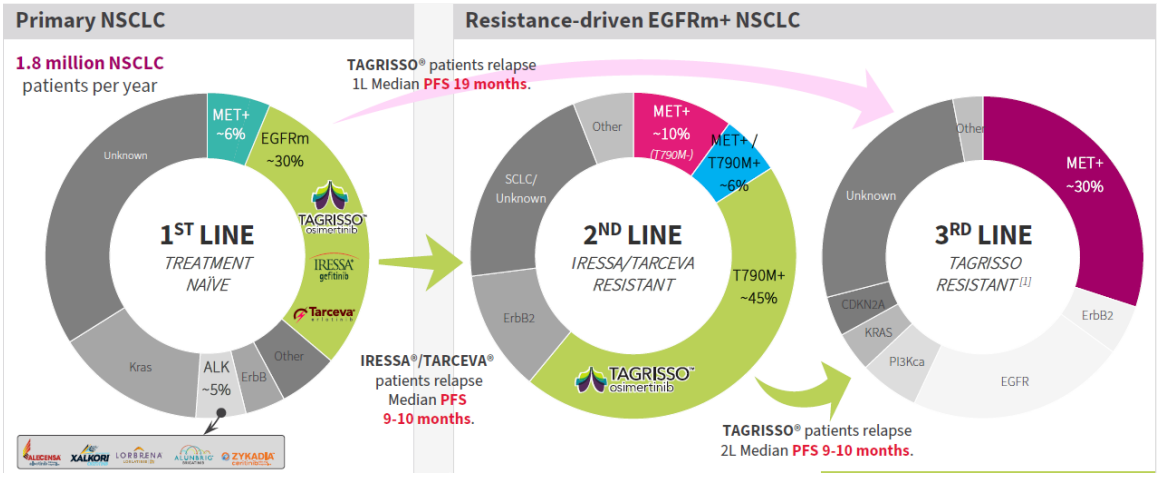
Figure 8: Cancer incidences and MET amplification, mutation and over-expression in solid tumors

Indication	MET over-expre. (%)	MET amplifi (%)	MET mutation (%)	Incidences ex. China (000')	Incidences in China (000')
NSCLC	39	4/16/30*	2	1,876	786
Colorectal	65	10	3	1,881	453
Prostate	54/83*	0	1	1,414	114
Gastric cancer	41	10	1	1,089	470
Head & neck	46*	17-39	11	932	143
Esophagus	92	8	1	604	290
Clear cell renal	35	54	n.a.	301	60
Papillary renal	55	64	17-33	49	4

Sources: Frost & Sullivan, CMS(HK)

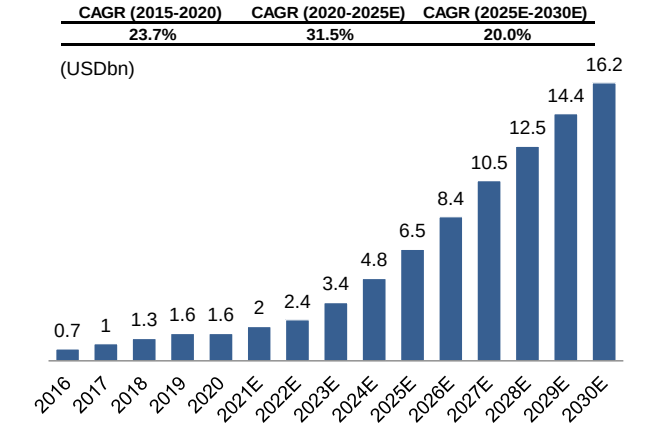
Below is an illustration of the addressable market for MET inhibitors in MET-driven NSCLC. T790M mutation is the primary mechanism of EGFR resistance and occurs in approximately 50% of patients treated with 1st generation anti-EGFR drugs (Gefitinib, Erlotinib, and Icotinib). The second most common mechanism of EGFR resistance next to T790M mutation is MET dysregulation, which occurs 5-26% of NSCLC cases. Specifically, 5% of patients develop MET gene amplification after receiving first- and second- generation EGFR TKIs (source: D. Westover, et al. Annals of Oncology 29 (Supplement 1): i10–i19, 2018). Meanwhile, in AstraZeneca's FLAURA trial, preliminary ctDNA NGS study revealed that MET-amplification was the most common resistance mechanism (15% of patients) following 1st line Tagrisso treatment. Meanwhile, 19% of patients in AZ and HCM's AURA3 trial had MET-amplification after 2nd line Tagrisso treatment. Such data suggest that the appearance of MET gene amplification could be more frequent following administration of third-generation EGFR TKI compared to earlier generations EGFT TKI.

Figure 9: MET inhibitor's global opportunities in MET+ NSCLC



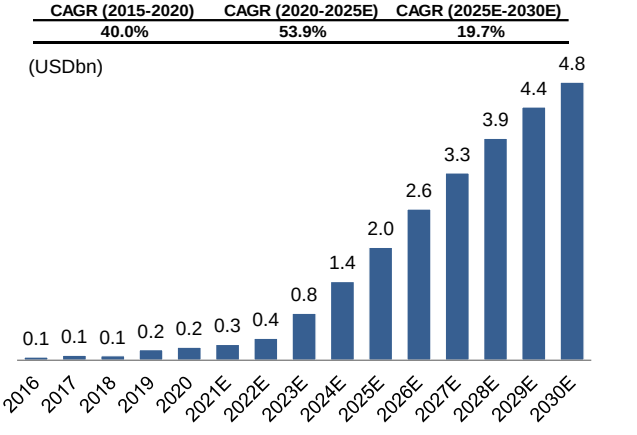
Source: Company data

Figure 10: c-MET global market size (USDmn)



Source: F&S

Figure 11: c-MET China market size (USDmn)



Source: F&S

Clinical data by indication

Savolitinib is currently in a global registrational study (SAVANNAH) in combination with osimertinib (EGFR inhibitor) for the treatment of MET+ NSCLC following prior treatment with osimertinib. In addition to this osimertinib combination, AZN/HCM are studying savolitinib in combination with Imfinzi (AZN's PD-L1 antibody) in patients with renal cell carcinoma (papillary cell) (CALYPSO).

Beyond these partnerships with AZN, HCM is evaluating savolitinib as a monotherapy and in combination with chemo (paclitaxel) in patients with MET+/MET over-expression gastric cancer (China). Other studies include a study of savolitinib as a monotherapy in prostate cancer, MET Exon 14 deletion NSCLC, and in combination with Iressa in 2L EGFR-mutant, Iressa refractory MET+ NSCLC.

Figure 12: Savolitinib trial summary in ex-China

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
Savo. + Tagrisso	NSCLC	2/3L EGFRm, Targrisso ref.:	SAVANNAH (Ph2)	Global	To start in 2H21E		
Savo. + Imfinzi	PRCC	MET+	SAMETA (Ph3)	Global	Trial in planning (start in 2H21E)		
Savo. + Imfinzi	PRCC	All	CALYPSO (Ph2)	UK/Spain	Ph2 data (ASCO21)		
	CRCC	VEGFR TKI ref	CALYPSO (Ph2)	UK/Spain	Ph2 data (ASCO21)		
Savolitinib	GC	MET+	VIKTORY (Ph2)	S Korea	Data published in journals		
Savolitinib	CRC	MET+	(Ph2)	US			

Source: Company data; Note: POC: proof-of-concept, NSCLC: non-small lung cancer, PRCC: papillary renal cell carcinoma, CRCC: clear renal cell carcinoma, GC: gastric cancer, ref: refractory

Figure 13: Savolitinib trial summary in China

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
Savolitinib	NSCLC	MET Exon 14 skipping	(Ph2)	China	China NDA approved in Jun 2021		
Savo. + Tagrisso	NSCLC	2L EGFR TKI ref., MET+	SACHI (Ph3)	China	Trial in planning (FPI in 2H21E)		
Savo. + Tagrisso	NSCLC	Naive MET + EGFRm	SANOVO (Ph3)	China	Trial in planning (FPI in 2H21E)		
Savolitinib	GC	2L, MET+	(Ph2)	China	FPI in July 2021		

Source: Company data; Note: POC: proof-of-concept, NSCLC: non-small lung cancer, GC: gastric cancer, ref: refractory, FPI: first patient in

AstraZeneca collaboration recap

In Dec 2011, HCM out-licensed worldwide rights of savolitinib to AstraZeneca (AZN). Under the pact (including an amendment made in 2016), AZN is responsible for development costs ex-China while HCM share development costs for savolitinib in China. HCM also contributes up to USD50mn in ex-China development costs for savolitinib in pRCC (span over three years). Subject to approval of savolitinib in pRCC, HCM is entitled to receive tiered 14%-18% royalties on all sales ex-China, which would step down to 10.5%-14.5% once aggregate sales of savolitinib reach USD5bn. Within China market, HCM is entitled to receive a 30% royalty rate on all savolitinib sales.

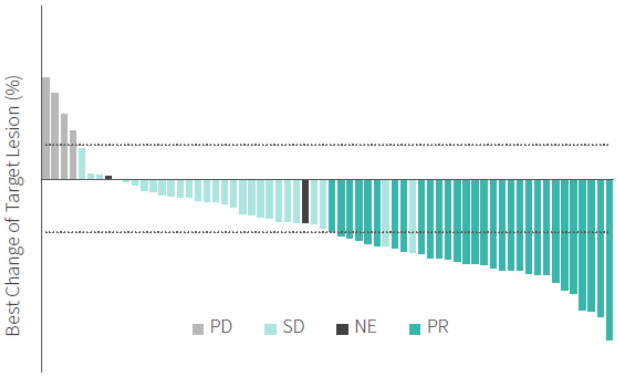
MET exon 14 skipping NSCLC

Co.'s received conditional approval from the China CDE for the indication of METex14m NSCLC. The regulatory decision is supported by data from a ph2 trial (NCT02897479) done in China that enrolled patients with NSCLC who harbored this mutation, including those with the more aggressive pulmonary sarcomatoid carcinoma (PSC) subtype. Data in ASCO21 showed IRC-accessed ORR of 49.2% (42.9% in the full analysis set) with 9.6mo duration of response (DOR). The PFS and OS data were not yet mature at the time of presentation. However, at 50% maturity, the median PFS was 6.9 months, and at 45.7% maturity, the median OS was 14.0 months.

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

China Phase II registration [1]	Efficacy Evaluable (N=61)	Full Analysis (N=70)
ORR, % [95% CI]	49.2% [36.1–62.3]	42.9% [31.1–55.3]
DCR, % [95% CI]	93.4% [84.1–98.2]	82.9% [72.0–90.8]
mDoR, mo	8.3 [5.3–16.6]	8.3 [5.3–16.6]

Source: Company data



Source: Company data

Two competitors' MET-targeted TKIs, namely capmatinib and tepotinib, are approved in the METex14m NSCLC. We note that savolitinib demonstrated comparable ORR in NSCLC patients in the similar setting with numerical better safety profile, while caveating that such cross-trial comparison is difficult as some trials have different enrollment criteria. Meanwhile, we reckon crizotinib's efficacy profile is not competitive comparing with c-MET class drug, despite a breakthrough designation received from the FDA in 2018.

Figure 15: Summary of c-MET inhibitors in the space of MET exon 14 skipping NSCLC

Company	**Novartis**	**Merck**	**HutchMed**	**Pfizer**		
Generic name	**Capmatinib**	**Tepotinib**	**Savolitinib**		**Crizotinib**	
MoA	c-MET	c-MET	c-MET		c-MET/ALK/ROS	
Indication	exon 14m NSCLC	exon 14m NSCLC	exon 14m NSCLC	exon 14m NSCLC	ALK+ NSCLC	ROS+ NSCLC
Approval (Yr)	- US cond. (2020)	- US (2021) JP (2020	- China cond. (2021)	BTD (2018)	- US / China (2011/13)	- US / China (2016/17)
Study Phase	Phase 2	Phase 2	Phase 2	Phase 1	Phase 1	Phase 1
Allocation	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized
Intervention Model	Single	Single	Single	Single	Single	Single
Selected Dose	400mg QD	450mg QD	600mg/400mg QD	250mg BID	250mg BID	250mg BID
Study Arms	Capma naive & treated (n=28 & 69)	Tepo naive & treated (n=69 & 83)	Savo naive & treated (n=61)	Crizotinib (n=65)	Crizotinib treated & LDT tested (n=119 & 136)	Crizotinib (n=50)
Efficacy data						
Primary Outcome						
mPFS (month)	12.4 & 5.4	12.3	NR	7.3	n.a.	n.a.
mOS (month)	20.8 & 13.6	n.a.	NR	20.5	n.a.	n.a.
Secondary Outcome						
ORR (%)	68 & 41	43 & 43	49.2	32	50 & 61	66
mDOR (month)	12.6 & 9.7	10.8 & 11.1	NR	n.a.	10.5 & 12.0	18.3
Safety profile						
AEs (%)	SAEs: 51	SAEs: 45	≥G3 41		SAEs: 38	SAEs: 38
Administrative Info						
NCT Number	NCT02414139	NCT02864992	NCT02897479	NCT00585195	n.a.	NCT00585195
Study ID	GEOMETRY mono-1	VISON	2016-504-00CH1	PROFILE 1001	Subpart H & E	PROFILE 1001
Data Source	FDA	FDA	ASCO 2020	Nature Medicine	FDA	FDA, NEJM

Sources: FDA, NEJM, Company data, CMS (HK)

EGFR TKI refract. NSCLC w/ MET amplification

The most important developmental program for savolitinib is in 2L/3L EGFR-mutant (EGFRm), Tagrisso refractory, MET+ NSCLC in combination with Tagrisso, which was first studied in the TATTON A/B studies.

At the WCLC 2020, HCM reported the full data of TATTON study that evaluates savolitinib plus Tagrisso in the patients harboring MET gene amplification and EGFR mutations who progressed after EGFR therapy. We think the most important data came from the cohort 2 of TATTON B study which covers the MET+ patients after prior treatment with 3rd generation EGFR TKI (Tagrisso). Currently no other competitors' c-MET inhibitors trials cover MET+ Tagrisso failure patients, to our knowledge (please refer to figure 19 for the c-MET plus EGFR TKI NSCLC trial landscape).

TATTON B comprised of three cohorts: the patients with prior treatments of 3rd generation EGFR TKI (Part B1) and the patients who not received prior treatment of a 3rd generation EGFR TKI (T790M-/+) (Part B2/B3). HCM reported that the ORR in Part B1 and B2/B3 were 33% and 65%/67% respectively, demonstrating savolitinib + osimertinib combo could provide clinical benefit toward either 3rd GEN EGFR-TKI treatment naive or treated patients.

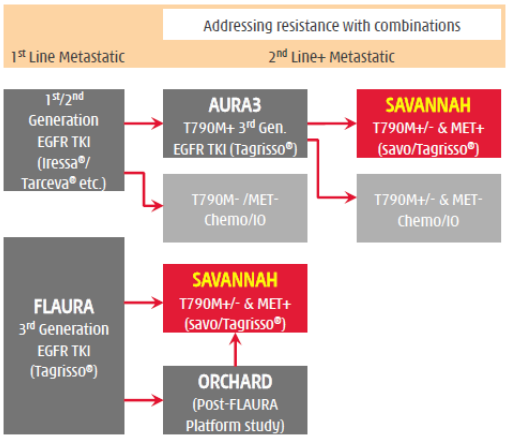
Figure 16: Savolitinib's Ph1b TATTON study (NCT02143466)

Study	**TATTON B**			**TATTON D**
	Part B1	**Part B2**	**Part B3**	**Part D**
Dosing	**Savo 600mg** + TAGRISSO 80mg			**Savo 300mg** + TAGRISSO 80mg
Indication	Prior 3d gen EGFR-TKI	No Prior 3d gen EGFR-TKI (T790M-)	No Prior 3d gen EGFR-TKI (T790M+)	No Prior 3d gen EGFR-TKI (T790M-)
Study arm (eval./total)	(n=69/180)	(n=51/180)	(n=18/180)	(n=42/180)
Efficacy data				
ORR (%)	33%	65%	67%	62%
DCR (%)	75%	88%	100%	93%
mPFS (month)	5.5	9.4	11.1	9.0
DoR (month)	9.5	10.7	11.0	9.7
Safety profile				
≥G3 AE (%)		62		50

Source: Company data, CMS (HK)

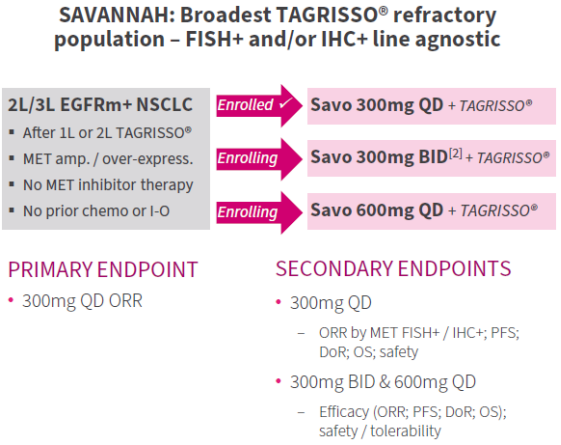
Based on the TATTON B data, HCM and AstraZeneca have initiated the SAVANNAH study with registration intent. **SAVANNAH** is a ph2 single-arm study (N=172) of savolitinib + osimertinib, in 2L NSCLC patients with MET gene amplification and EGFR mutations who have progressed following 1L osimertinib treatment. We note that the SAVANNAH study is closely aligned with AZ's FLAURA, AURA3 and ORCHARD studies with the aim to expand the treatment options of Tagrisso combinations in more NSCLC patients with acquired EGFR resistance. HCM expects data readout of SAVANNAH study in 2H21E, which should pave the way for a global confirmatory Ph3 trial in 2H21E.

Figure 17: SAVANNAH study is well aligned with AZ's other studies on Tagrisso



Source: Company data

Figure 18: SAVANNAH ph2 trial design



Source: Company data

Figure 19: Savo+osimer showed promising clinical efficacy in NSCLC patients w/ EGFR acquired resistance*

	Combo w/ 3rd Gen EGFR TKI				Combo w/ 1st/2nd Gen EGFR TKI		
Company	HCM	HCM	Novartis	Merck	HCM	Novartis	Merck
Study ID	TATTON (B1)	SAVANNAH	2014-000726-37 (Group 1)	INSIGHT 2	D5080C00001	CINC280X2202	INSIGHT
Study Phase	Ph1b	Ph2	Ph1/2	Ph2	Ph1	Ph1b/2	Ph1b/2
Trial design							
Indication	2L+ NSCLC patients w/ acquired resistance						
Treatment	Savo+osimer	Savo+osimer	Capma+nazarti	Tepo+osimer	Savo+gefiti	Capma+ gefiti	Tepo+gefiti (vs chemo)
Dosing	600mg+80mg QD	300mg+80mg QD	400mg BID+ 100mg QD	500mg+80mg QD	600/800mg+ 250mg QD	400mg BID+ 250mg QD	500mg+250mg QD (vs chemo)
Enrollment (evaluable/total)	69/180	259	52/177	120	64	161	55
Efficacy data							
ORR (%)	33	n.a.	28.8	n.a.	25	27 (overall) 47 (GCN>6)	68 vs 33 (IHC3+) 21.2 vs 4.2 (GCN>5)
mPFS (month)	5.5	n.a.	5.6	n.a.	n.a.	5.5 (GCN4-6) 5.5 (GCN≥6)	8.3 vs 4.4 (IHC3+) 21.2 vs 4.2 (GCN>5)
DoR (month)	9.5	n.a.	6.3	n.a.	n.a.	n.a.	n.a.
mOS (month)	n.a.	n.a.	n.a.	n.a.	TBC	13.9	37.3 vs 17.9 (IHC3+)
Safety profile							
AEs (%)	SAE: 49	n.a.	n.a.	n.a.	≥G3: 32	G3/4: 32%	≥G3: 62 (vs 52)
Admin Info							
NCT Number	NCT02143466	NCT03778229	NCT02335944	NCT03940703.	NCT02374645	NCT01610336	NCT01982955
Data Source	Company	Company	ESMO 2020	ASCO 2021	WCLC 2017	ASCO 2018/2021	ESMO 2018

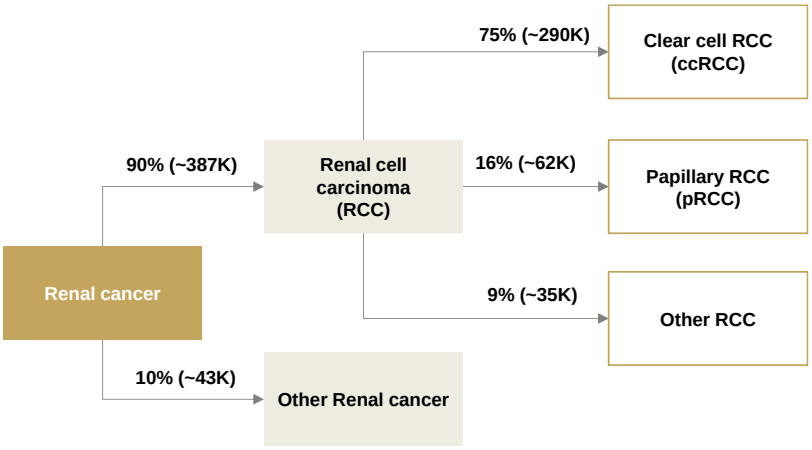
Sources: clinicaltrial.gov, Note competitors trials not cover pts that have progressed after the treatment with 3rd generation EGFR TKI.

Savolitinib in papillary renal cell carcinoma (pRCC)

Beyond NSCLC, savolitinib has exhibited potential for providing antitumor benefit based on pre-clinical studies as MET gene expression was commonly found in pRCC patients.

pRCC is the second most common type of RCC following clear-cell RCC (ccRCC), it accounts for approximately 10-15% of all new cases of RCC, affecting about c.11,000 people in the U.S and c.10,000 in China. (source: Basma Greef, et al. British Journal of Cancer (2016) 115, 505–516) MET signaling pathway has been shown to associate with the development of pRCC. Despite being a reasonable pharmaceutical target, no MET inhibitor has been FDA secured for pRCC therapy.

Figure 20: Subtypes of RCC



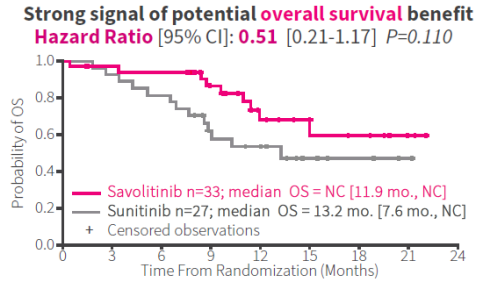
Sources: JAMA, NEJM, CMS (HK)

As per Carlsson, et al's study on the Journal of Applied immunohistochemistry & Molecular Morphology (AIMM), PD-L1 expression on pRCC tumor cells can result in poor prognosis. In ASCO 2021, Co. reported the data of savolitinib in combination with Imfinzi (durvalumab, PD-L1 inhibitor) in one arm of AstraZeneca's CALYPSO trial (NCT02819596). The study demonstrated an ORR of 57% and mPFS of 10.5mo in 14 evaluable patients with MET-driven pRCC with no new safety signals (prior data from 2019 showed 37% patient (15 of 41 patients) experienced grade 3-4 TRAEs and 3 patients discontinued due to AEs). Such efficacy and safety data were superior to its rivals forentinib and tivatinib. Based on the encouraging ph2 CALYPSO data, Co. expects a subsequent ph3 SAMETA study initiation in 2H21E. If such efficacy is confirmed in larger trials, Imfinzi/savolitinib combo may have chances of becoming a treatment option in 1L pRCC.

Previously in JAMA Oncol. 2020, savolitinib monotherapy demonstrated an ORR of 27% and mPFS of 7.0 months in 60 evaluable patients with MET-driven pRCC, vs. sunitinib's 7% ORR and 5.6mo PFS. Meanwhile the study also showed 19% grade 3-4 TRAE and 8% of patients discontinuing the trial due to AE. Such efficacy and safety data were superior to its rivals forentinib and tivatinib. That said, the subsequent ph3 SAVOIR study to compare savolitinib monotherapy to sunitinib (standard-of-care for PRCC treatment) in the 2L setting might face challenge on patient enrollment, as sunitinib was heavily used off-label in 1L pRCC and it was difficult to recruit MET+ pRCC patients.

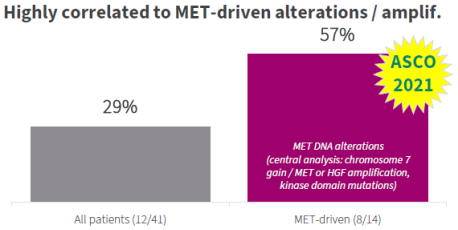
Figure 21: SAVOIR study (savo mono) data

SAVOIR [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]	



Sources: Company data, AstraZeneca

Figure 22: CALYPSO study (savo + durva) data



	All patients [2] (N=41)	MET-driven [3] (N=14)
ORR	29%	57%
mPFS	4.9 mo.	10.5 mo.
mOS	12.3 mo.	27.4 mo.
PFS @ 12 mo.	31.1% [16.8-46.9]	TBD
OS @ 12 mo.	52.1% [35.0-66.8]	TBD

Sources: Company data, ASCO

Figure 23: Savolitinib + anti-PDL1 drugs showed superior ORR versus other C-MET inhibitors in pRCC

	PD-1/L1 combo	Monotherapy				
Study ID	**CALYPSO**	**SAVOIR**	**PAPMET (Savo cohort)**	**D5082C00002**	**S1107 (Arm2)**	**MET111644**
Study Phase	Ph2	Ph3	Ph2	Ph2	Ph2	Ph2
Trial design						
Treatment	**Savo+Durvalu**	**Savo (vs Suniti)**	**Savo**	**Savo**	**Tivanti+Erloti**	**Foretinib (halted)**
Indication	1L pRCC	pRCC	pRCC	1/2L pRCC	pRCC	pRCC
Dosing	600mg QD+ 1500mg Q4W	600mg QD (vs 50mg QD)	600mg QD	600mg QD	360mg BID+ 150mg QD	240mg (5/9 dosing) or 80mg QD
Enrollment (evaluable/total)	41/195	33 (vs 27)	Savo cohort: 29	99/109	55	74
Efficacy data						
ORR (%)	29 (overall) 57 (MET+)	27.0 (vs 7.0)	n.a.	7	0.0	13.5 (overall)
mPFS (month)	4.9 (overall) 10.5 (MET+)	7.0 (vs 5.6) HR: 0.71, P=0.110	n.a.	6.2 (MET+) 1.4 (MET-)	3.9	9.3 (overall)
mOS (month)	12.3 (overall) 27.4 (MET+)	NR (vs 13.2) HR: 0.51, P=0.110	n.a.	n.a.	n.a.	n.a.
Safety profile						
AEs (%)	G3/4: 37%	≥G3: 42 (vs 81)	G3/4: 39%	≥G3: 19	SAE: 64	SAE: ~56
Administrative Info						
NCT Number	NCT02819596	NCT03091192	NCT02761057	NCT02127710	NCT01688973	NCT00726323
Data Source	ASCO 2021	Company	ASCO 2017	ASCO 2017	Clinicaltrial.gov	Clinicaltrial.gov

Sources: ASCO, Company

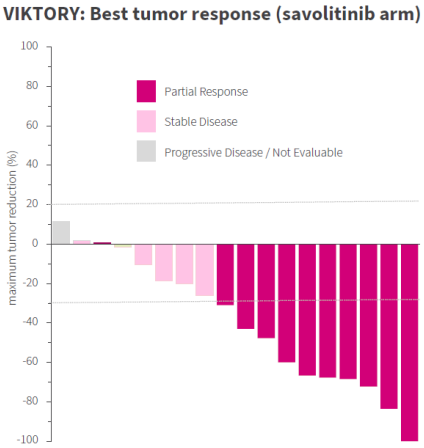
Savolitinib in GC

Preclinical and clinical studies have found that HGF/c-MET pathway plays an important role in the growth and metastases of gastric cancer cells. In addition, MET+ gastrointestinal disease progression are more aggressive and result in a significant shorter survival time of patients (mOS of MET amp. +VE vs –VE: 28.6mo vs 68.7mo).

Poor prognosis of traditional therapies (i.e. chemo) and mixed results of I/O mono therapies for gastric cancer treatment, have pushed scientists to search for more individualized targeted therapies.

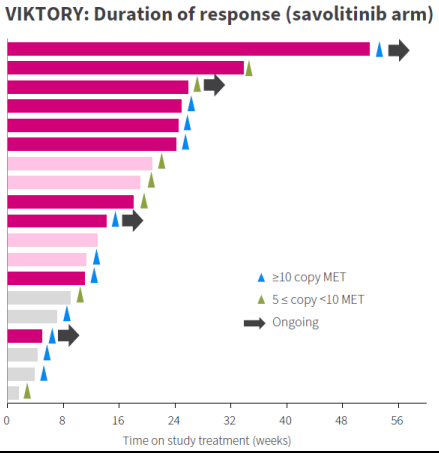
Given the unmet medical need, particularly in eastern Asian countries, Co. has completed Ph1 **VIKTORY** trial in China and S.Korea and yielded encouraging antitumor activities in patients who failed in frontline chemotherapy (below table). Co. is initiating a potentially registrational Ph2 for 2L MET+ GC patients in 2H21E in China.

Figure 24: Pts tumor reduction, VIKTORY (savo arm)



Source: Company data

Figure 25: DoR of VIKTORY trial (savo arm)



Source: Company data

Savolitinib in other solid tumors

Co. and investigators thus are also exploring the therapeutic value of savolitinib in other solid tumors with excessive activations of c-MET, including colorectal cancer (CRC) and esophageal squamous-cell carcinoma (ESCC).

Competitive landscape

Depending on the type of interaction with the ATP binding site, c-MET inhibitors can be classified into two types (I and II). Type I inhibitors tend to be more selective for MET than type II multi-kinase TKIs inhibitors (source: Porter J. Expert Opin Ther Pat. 2010 Feb; 20(2):159-77). The three approved type Ib selective MET inhibitors are capmatinib, tepotinib and savolitinib, which are shown to be more selective in MET binding and has fewer off target effects than type II inhibitors, such as Cabometyx (cabozantinib) and Xalkori (crizotinib). Given savolitinib's selectivity to MET, we see it as favorably positioned vs. these multi-kinase inhibitors.

Figure 26: Savolitinib is a MET specific inhibitor

Agents	Company	MoA	IC50 (nM) for c-MET	Indications approved	Indications under study
Commercial					
Capmatinib	Novartis	c-MET	0.13nM	METex14m NSCLC	RCC/CRC/HCC, etc
Cabozantinib	Exelixis	c-MET/VEGFR2 RET/Kit/AXL	1.3nM	RCC/HCC	RCC/CRC/GC, etc.
Tepotinib	Merck	c-MET	4.0nM	METex14m NSCLC	CRC/HCC
Savolitinib	HutchMed	c-MET	5.0nM	METex14m NSCLC	RCC/CRC/HCC, etc
Crizotinib	Pfizer	c-MET/ALK	11.0nM	NSCLC/lymphoma	RCC/CRC/HCC, etc
Clinical stage					
Glumetinib	SH Haihe	c-MET	0.42nm	n.a.	NSCLC
SAR125844	Sanofi	c-MET	4.2nM	n.a.	NSCLC/ST
Sitravatinib	Mirati	c-MET/HGFR VEGFR/PDGFR	20.0nM	n.a.	Liposarcoma
TQ-B3139	SBP	c-MET/ALK/ROS	n.a.	n.a.	NSCLC
Bozitinib	Apollomics	c-MET	n.a.	n.a.	NSCLC/HCC/RCC/ST
Tivantinib	Arqule	c-MET	100.0nM	Suspended	
Foretinib	GSK	c-MET Tie/VEGFR3/RON	0.4nM	Suspended	
Glesatinib	Mirati	c-MET	1.0nM	Suspended	

Sources: Selleck Chemicals, clinicaltrial.gov, Evaluate Pharma

CMS estimates

We model for savolitinib sales in NSCLC (CN, US/EU), pRCC (US/EU) and gastric cancer (China), and ongoing clinical development. Beyond the exon 14 skipping NSCLC, we think the biggest market opportunity lies in the combination therapy with osimertinib (Tagrisso), a 3rd Gen EGFR TKI developed by AstraZeneca with global sales of ~USD4.3bn during FY20. We think osimertinib's market presence will continue to grow as it is expanding its studies into earlier treatment setting (i.e. Ph3 FLAURA2 for 1L NSCLC) and savolitinib as a combo drug will benefit.

NSCLC (70% POS China / 70% POS ex-China): We model for peak penetration of savolitinib in 2L/3L NSCLC of 25% China/12% ex-China and assume duration of therapy in-line with mPFS from prior clinical study of savolitinib + Tagrisso at 7.0mo in 2L+. We assume initial monthly post-NRDL (estimated in 2021E) price in China of USD1.5K, falling to USD1.1K post peak sales (estimated in 2025E), and in the US we assume net price of USD13.4K (in-line with EGFRi market). Together this implies unadjusted peak sales of USD939mn.

pRCC (70% POS ex-China): Papillary renal cell carcinoma accounts for ~10-15% of renal cell cancers, with an ~8% rate of MET+ within that population. We assume peak penetration of savolitinib (in combination with Imfinzi) of 5% in the US, and estimate duration of therapy of 10.5mo (consistent with clinical data) which implies peak sales of USD139mn.

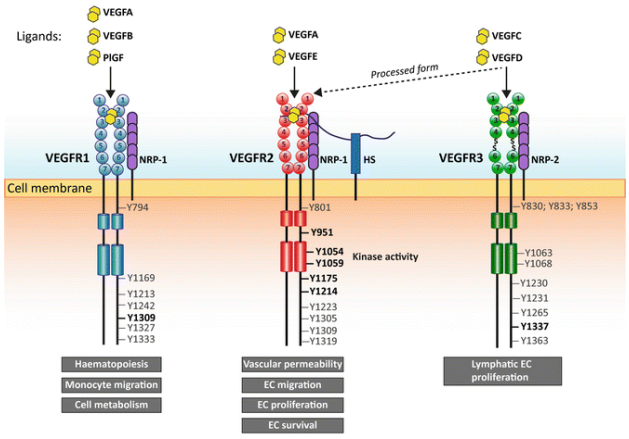
Gastric Cancer (60% POS China): We assume peak penetration of 10% in MET+ gastric cancer (China/US) and estimate a 7.7mo duration of therapy, implying USD174mn in peak sales.

Fruquintinib (VEGFR 1/2/3 inhibitor)

Fruquintinib is an in-house developed, selective inhibitor of the vascular endothelial growth factor receptor (VEGFR) tyrosine kinase to prevent angiogenesis. Anti-angiogenesis therapies are well-established in the treatment of various solid tumors, including approved VEGFR1/2/3 inhibitors (Stivarga, Sutent, Nexavar) as well as Biologics (Avastin and Cyramza).

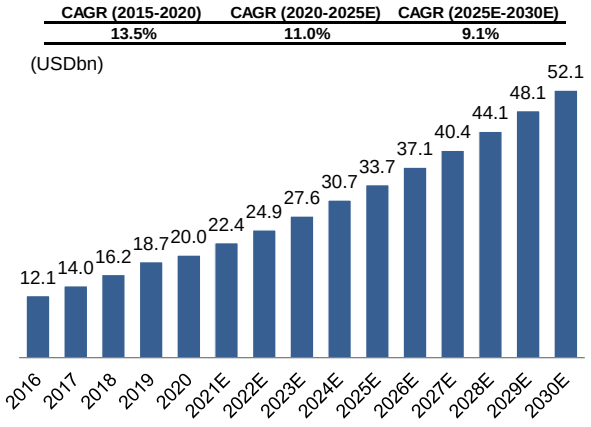
Fruquintinib obtained NMPA's approval on 3L metastatic colorectal cancer (mCRC) in China in September 2018. It has also been included in the NRDL since 2019 following its approval in 2018. Co. regained the China commercial initiatives from Eli Lilly after a collaboration agreement amendment in October 2020. Eli Lilly will pay HCM an estimated 70-80% of ELUNATE sales in the form of royalties, manufacturing costs and service payments. Meanwhile, In addition, HCM continues to develop fruquintinib for additional indications (NSCLC, gastric cancer, colorectal cancer, and other advanced solid tumors) and geographic expansion.

Figure 27: An illustration of the mechanisms of action of VEGF(R) inhibitors



Source: Encyclopedia of Signaling Molecules

Figure 28: VEGF global market size (USDbn)



Source: F&S

Clinical data by indication

Fruquintinib was approved by the China CDE for 3L mCRC in September 2018. In addition, HCM has expanded fruquintinib into the US/EU with a Ph3 FRESCO study in this population. While fruquintinib failed the 3L NSCLC trial (FALUCA) in November 2018, we think its main opportunity lies in the combination with PD-1 in solid tumors. Currently, HCM initiated combination therapies with three varied PD-1/L1 products or candidates, including combining fruquintinib with Innovent and Genor Biopharma's PD-1 in China and with BeiGene's tislelizumab in the U.S. In addition, Co. is also exploring therapeutic value in 2L GC with paclitaxel combo in gastric cancer (Ph3 FRUTIGA).

Figure 29: Fruquintinib ex-China trial summary

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
Fruqu	CRC	Refractory	FRESCO-2 (Ph3)	US/EU/Japan	Phase initiated		
Fruqu	BC		Ph2	US			
Fruqu + tisleli (PD-1)	TNBC		Ph1b	US			
Fruqu + tisleli (PD-1)	ST		Ph1b	TBD			

Source: Company data; Note: POC: proof-of-concept, CRC: colorectal cancer, BC: breast cancer, TNBC: triple negative breast cancer, ST: solid tumors

Figure 30: Fruquintinib China trial summary

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
Fruqu	CRC	≥3L; chemo refractory	FRESCO (Ph3)	China	China NDA approved in Sep 2018		
Fruqu + chemo	GC	2L	FRUTIGA (Ph3)	China	Topline data expected in 2H22E		
Fruqu + toripa (PD-1)	CRC/EMC/ RCC/HCC		Ph1b/2	China	Ph1b/2 ongoing		
Fruqu + toripa (PD-1)	GI tumors		Ph1b/2	China	Ph1b/2 ongoing		
Fruqu + gepta (PD-1)	CRC		Ph1b	China	Ph1b ongoing		
Fruqu + gepta (PD-1)	NSCLC		Ph1b	China	Ph1b ongoing		

Source: Company data; Note: CRC: colorectal cancer, GC: gastric cancer, EMC: endometrial cancer, RCC: renal cell cancer, HCC: hepatocellular carcinoma, GI: gastrointestinal, NSCLC: non-small cell lung cancer

Eli Lilly (LLY) collaboration recap

In October 2013, HCM entered into partnership with LLY to develop, manufacture, and commercialize fruquintinib in China and Hong Kong markets. The companies subsequently amended this agreement in December 2018, which entitles HCM to greater ownership of the development and commercial rights to fruquintinib. As of FY20, LLY has paid USD37mn in milestone payments and USD53.2mn in development cost reimbursement.

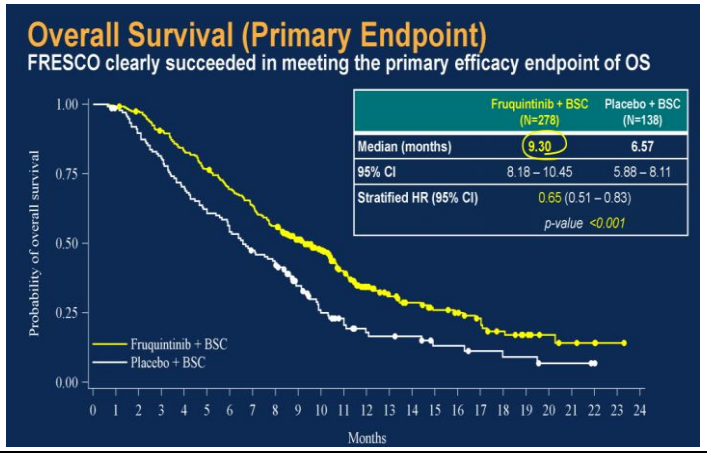
In July 2020, HCM and LLY announced an amendment to the 2013 License and Collaboration Agreement on fruquintinib. The 2020 amendment covers the expansion of HCM's role in the commercialization of ELUNATE in China. Under the terms of the 2020 Amendment, LLY will pay HCM an estimated total of 70%-80% of ELUNATE sales in the form of royalties, manufacturing costs and service payments. There is no upfront payment by LLY or HCM relating to this amendment. Ex-China, HCM retains all development and commercial rights to fruquintinib.

Fruquintinib in colorectal cancer

China NDA was supported by data from phase III trial (FRESCO), in 416 patients with locally advanced or metastatic CRC. Subgroup analysis was conducted in patients with prior targeted therapy (PTT) and those without (non-PTT). Median OS in fruquintinib vs. placebo treated group was 7.69 m and 5.98 m (HR=0.63, p=0.023). In non-PTT subgroup, the median OS was 10.35 m for fruquintinib vs 6.93 m for placebo (HR = 0.63, p = 0.01). The most common drug-related Grade ≥3 TEAEs of fruquintinib in PTT and non-PTT subgroup were hypertension (20.7% and 21.6%), hand-foot-skin reaction (7.2% and 13.2%) and proteinuria (5.4% and 1.8%).

CRC is the fifth most common type of cancer in China with 470k incidences in 2020 (source: WHO). Company estimated patient size for 3L CRC treatment is 83K in China and 81K in US/EU5/Japan. We think in this setting, fruquintinib should potentially compete with Stivarga (regorafenib), a multi-target inhibitor for VEGFR 1-3, PDGFRβ, Kit, RET and Raf-1. Despite Stivarga survival benefits with median OS of 6.4mo in regorafenib treated arm vs. 5mo in placebo arm (HR=0.77), it is worth to note that the drug was approved along with a black box warning of possible liver toxicity, which should likely limit its opportunities in mCRC.

Figure 31: China approval based on FRESCO trial



Sources: Company data, ASCO

In addition, fruquintinib has a clear regulatory pathway for global approval for 3L+ CRC global approval (FDA NDA and EMA MAA), supported by: 1) FRESCO China ph3 study; 2) FRESCO-2 global ph3 study, and, 3) a US/local-based Ph1b safety study. Fruquintinib received fast track designation (FTD) from the US FDA in 2020 and is eligible for a rolling review. We expect an US NDA approval of fruquintinib in 2H22E/1H23E.

Figure 32: Fruquintinib showed efficacy and safety advantages over regorafenib

Study ID	**FRESCO**		**CONCUR**		**CONCUR**		**CORRECT**	
Location	Mainland China		Greater China (Mainland, HK, TW)		Greater China, Vietnam, S. Korea		Global	
Treatment arms	**Fruqu**	Placebo	**Regora**	Placebo	**Regora**	Placebo	**Regora**	Placebo
Patient number	**278**	138	**112**	60	**136**	68	**505**	255
Efficacy data								
ORR (%)	**4.7**	0.0	**3.6**	0.0	**4.4**	0.0	**1.0**	0.4
pDCR (%)	**62.2**	12.3	**45.5**	6.7	**51.5**	7.4	**41.0**	14.9
mPFS (month)	**3.7**	1.8	**2.0**	1.7	**3.2**	1.7	**1.9**	1.7
mOS (month)	**9.3**	6.6	**8.4**	6.2	**8.8**	6.3	**6.4**	5.0
Safety profile								
>G3 TEAE (%)	**61.1**	19.7	**69.6**	46.7	**n.a.**	n.a.	**n.a.**	n.a.
SAEs (%)	**15.5**	5.8	**31.3**	26.7	**n.a.**	n.a.	**46.4**	40.7
Box Warning	**No**		**Liver toxicity black-box warning**					

Sources: Company data, ASCO

PD-1 inhibitor combinations

HCM is also exploring combination therapies with three varied PD-1/L1 products or candidates, including combining fruquintinib with Innovent and Genor Biopharma's PD-1 in China and with BeiGene's tislelizumab in the U.S. We believe the PD-1 inhibitor combination strategy will add strength to build up fruquintinib longer-term growth and maximise value creation.

Figure 33: Co.'s ongoing Fruquintinib combo studies

Treatment	Indication	Location	Stage	Enrollment (n)
Fruqu + PD-1 (sintili)	2L+ CRC	China	Phase 2	~35
	HCC/EC/RCC/GI	China	Phase 1b/2	~120
Fruqu + PD-1 (geptano)	2L/2L+ CRC/	China	Phase 1b	~15
	NSCLC	China	Phase 1b	~15
Fruqu + PD-1 (tisleli)	TNBC	US	Phase 1b	~80
	Solid tumors	TBD	Phase 1b	~60

Sources: Company date, CMS (HK)

Figure 34: Data of Co's key combo studies

	Fruq mono	**Fruq + PD-1/L1**			**Lenva + PD-1/L1**
Study ID	FRESCO	n.a.	Gxplore-012-1	2020-013-00US3	LEAP-005
Study Phase	Phase 3	Phase 2	Phase 1b	Phase 1b	Phase 2
Trial design					
Treatment	**Fruq**	**Fruq + Sintili**	**Fruq + Geptano**	**Fruq + Tisleli**	**Lenva + Pembro**
Indication	2L+ CRC	2L+ CRC	2L/2L+ CRC	TNBC/solid tumors	2L+ CRC
Dosing (Fruq)	5mg QD	5mg QD	4mg QD	n.a.	20mg QD
Enrollment (evaluable/total)	278	22	15	n.a.	32
Efficacy data					
mPFS (month)	3.7	6.9	7.3	n.a.	2.3
mOS (month)	9.3	11.8	NR	n.a.	7.5
ORR (%)	4.7	27.3	26.7	n.a.	21.9
DCR (%)	62.2	95.5	80.0	n.a.	46.9
Safety profile					
AEs (%)		n.a.	n.a.	n.a.	n.a.
Administrative Info					
Cut off date	Jan 2017	Apr 2021	Dec 2020	n.a.	Apr 10, 2020
NCT Number	XXX	NCT04179084	NCT03977090	NCT04577963	NCT02811861
Data Source	Company	Company	ASCO 2021	ASCO 2021	ASCO 2021

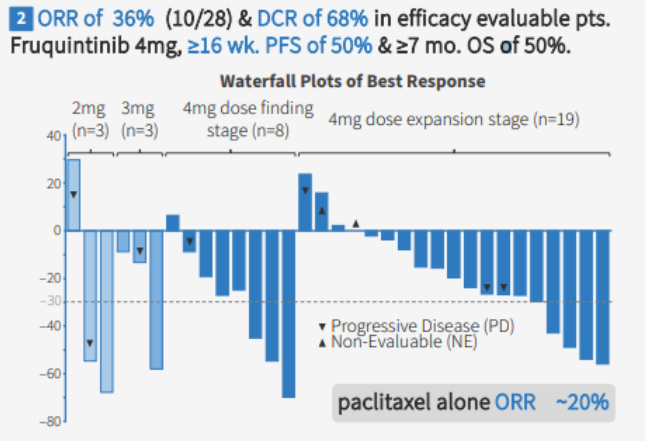
Sources: Company date, CMS (HK)

Fruquintinib in other solid tumors

Co. and investigators are also exploring the therapeutic value of fruquintinib and paclitaxel combo therapy in gastric cancer. Co. published the data of a Ph1/2 combo study for the indication of 2L gastric cancer at ASCO GC Symposium in Jan 2017. 28 of 32 enrolled patients were evaluable, with an ORR of 36% (vs paclitaxel mono of 20%).

Back by the positive ORR data from the above study, the Ph3 FRUTIGA trial will continue to explore the fruquintinib plus paclitaxel combo in 2L GC. Co will complete FRUTIGA study patient enrollment (~700 patients) by YE21E. Co. is expected to release top line data and to submit NDA to the NMPA by 2H22E.

Figure 35: ORR data of Ph2 study to support Ph3 FRUTIGA initiation



Source: Company data

CRC is the fifth most common cancer in globally with 1,089K incidences (o/w 470K from China) in 2020 and ~769K annual deaths. Company estimated patient size for 2L GC treatment is 234K in China and 107K in US/EU5/Japan.

We think in this setting, fruquintinib + paclitaxel should be potentially competitive against other 2nd line therapies, such as 1) reintroduction of platinum-based chemo, 2) maintenance of trastuzumab post-progression (ORR: 9.1%, Fu et.al, Onco Targets Ther. 2018), 3) ramucirumab + chemo combo (ORR: 25%, Chau et.al, Cancers (Basel) 2020), and 4) ramucirumab monotherapy.

Competitive landscape

VEGF/VEGFR inhibition is a crowded landscape with multiple approved therapies in a range of advanced solid tumor types. These include but are not limited to TKIs (Sutent, Nexavar, Stivarga) and biologics (Avastin, Cyramza) which are approved in CRC, NSCLC, and GC. Fruquintinib showed potent inhibition of VEGFR-1, −2 and −3 (half maximal inhibitory concentration [IC_{50}] values were 33 nmol/L, 25 nmol/L and 0.5 nmol/L, respectively), and weak inhibition of RET, FGFR-1 and c-KIT kinases. In comparison with other VEGFR1/2/3 class TKI, fruquintinib is a more specific VEGFR inhibitor with weaker off-target inhibition, resulting in better drug tolerability as 60% of late stage CRC pts have liver metastases.

Figure 36: Fruquintinib & surufatinib both unique VEGFR TKIs with higher selectivity over its VEGFR peers

	1st Gen			2nd Gen			Next Gen	
Selectivity	Multiple targets			Relatively selective			Highly selective	Selective angio-immuno
Drug	Sunitinib	Sorafenib	Anlotinib	Tivozanib	Lenvatinib	Axitinib	**Fruquinitnib**	**Surufatinib**
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 kinase (IC50<100nm)	PDGFRα PDGFRβ c-KIT FLT3 RET CSF-1R	RAF B-RAF FLT P38 C-KIT RET	PDGFRα PDGFRβ FGFR1-4 C-KIT	PDGFRα PDGFRβ EphB2 c-KIT TIE-2	PDGFRα PDGFRβ FGFR1-4 RET c-KIT	PDGFRα PDGFRβ C-KIT	**none**	CSF-1R FGFR1 FLT3 TRKB
Frist Patent Expiration	Expired	Expired	Expired	Expired	Oct 2021	Apr 2025	2029	2030

Source: Company data

CMS estimates

We mainly model for fruquintinib sales in CRC (China, US/EU), gastric cancer (China) and other indications based on the current approvals and ongoing clinical development.

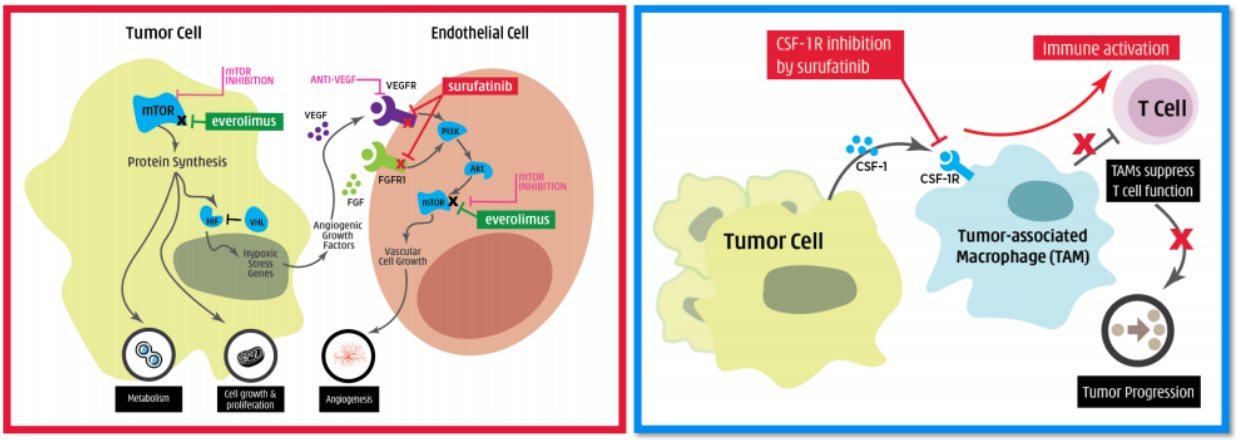
CRC (100% POS China / 50% POS ex-China): We estimate peak penetration in China of 15% (3L+ CRC), 7mo duration of therapy, assume USD81mn unadjusted in-market peak sales. Ex-China we estimate peak penetration of 3% (3L+ CRC) and assume USD13.2k for monthly US net pricing at peak which equates to USD329mn in unadjusted peak sales.

Gastric Cancer (70% POS China): We assume peak penetration to reach 15% market share of 2L gastric cancer in China and assume 4mo duration of therapy. This yields USD133mn in-market sales of ELUNATE in gastric cancer.

Surufatinib (VEGFR 1/2/3, FGFR1, CSF-1R inhibitor)

Surufatinib (Sulanda) is a VEGFR 1/2/3 (vascular endothelial growth factor receptor), FGFR1 (fibroblast growth factor receptor), CSF-1R (colony-stimulating factor-1 receptor) kinase selective inhibitor. The aforementioned three kinases play pivotal roles in 1) tumor angiogenesis (blood vessel formation of tumor), 2) antigen releases, and 3) tumor microenvironment regulations.

Figure 37: An illustration of the mechanisms of action of Co,'s surufatinib (Sulanda)



Source: Company data

In Dec 2020, China CDE approved surufatinib's NDA for the indication of non-pancreatic neuroendocrine tumor (ep-NET) based on the Ph3 SANET-ep study. In Jun, 2021, China CDE further granted NDA approval for the indication of pancreatic neuroendocrine tumors (NET-p) based on the Ph3 SANET-p study.

In ex-China, the FDA has accepted the filing of a NDA for surufatinib for advanced ep-/p-NET with a Prescription Drug User Fee Act (PDUFA) target action date of April 30, 2022. This consideration by the FDA follows a fast track designation granted to the agent in Apr 2020 for the treatment of ep-NET/p-NET. Surufatinib also received orphan drug designation (ODD) for the treatment of p-NET in Nov 2019. In addition, Co.'s MAA was recently accepted and validated by the European Medicines Agency (EMA).

Co. aims to participate in the 2021 NRDL negotiation for surufatinib under the indication coverage of ep-NET/p-NET, which would be the major catalyst for surufatinib in 2H21E.

Figure 38: Surufatinib ex-China trial summary

Treatment	Indication	Target patient	Phase	Locations	Dose finding/safety	POC	Registration
Suru	NET	Refractory	Ph3	US	US NDA accepted (FY22E launched expected)		
Suru	NET	Refractory	Ph3	EU	EU MAA accepted (FY22E launched expected)		
Suru	BTC		Ph1b	US	Ph1b ongoing		
Suru	STS		Ph1b	US	Ph1b ongoing		
Suru + tisleli (PD-1)	ST		Ph1b/2	US/EU			

Source: Company data; Note: POC: proof-of-concept, NET: neuroendocrine tumors, BTC: biliary tract cancer, STS: soft tissue sarcoma, ST: solid tumors

Figure 39: Surufatinib China trial summary

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
Suru	p-NET	All	SANET-p (Ph3)	China	China NDA approved in Dec 2020		
Suru	ep-NET	All	SANET-ep (Ph3)	China	China NDA approved in Jun 2021		
Suru	BTC	2L; chemo ref.	Ph2	China	Ph2 data (ASCO21)		
Suru + toripa (PD-1)	NEN/ESCC/BTC		Ph2	China	Ph2 data* (ASCO21)		
Suru + toripa (PD-1)	SCLC/GC/sarcoma		Ph2	China	Ph2 data* (ASCO21)		
Suru + toripa (PD-1)	TC/EMC/NSCLC		Ph2	China	Ph2 enrolling		
Suru + toripa (PD-1)	Solid tumors		Ph1	China			

Source: Company data; Note: ep/p: non-pancreatic/pancreatic, NEN: neuroendocrine neoplasm, ESCC: esophageal squamous cell carcinoma, SCLC: small cell lung cancer, GC: gastric cancer; Note: NEN and GC indication of suru + toripa (PD-1) study was presented at ASCO21*

Clinical data by indication

Surufatinib in ep-NET/p-NET

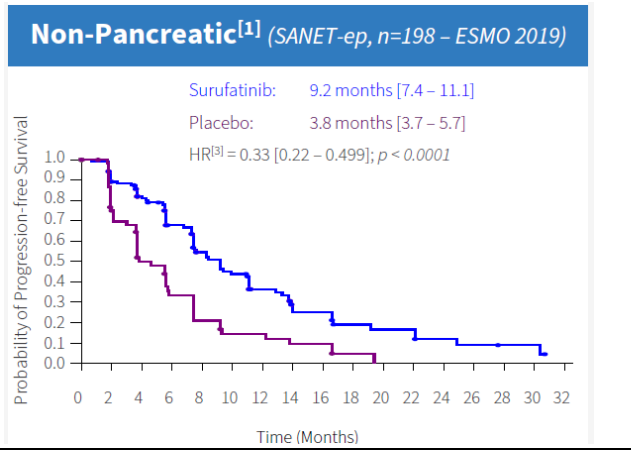
In Dec 2020, China CDE approved surufatinib's NDA for the indication of non-pancreatic neuroendocrine tumor (ep-NET). The NMPA approval of surufatinib (SULANDA) was based on results from the SANET-ep1 study, a ph3 trial (NCT02588170, N=273) in patients with advanced non-pancreatic NETs conducted in China. The study met the pre-defined primary endpoint of PFS at a preplanned interim analysis. Per ESMO 2019 and Lancet Oncology (Sep 2020), mPFS was significantly longer for patients treated w/ surufatinib than for patients in the placebo group (9.2mo vs. 3.8mo, HR 0.334; 95% CI: 0.223-0.499; p<0.0001). Surufatinib had an acceptable safety profile, with the most common ≥G3 TEAEs of hypertension (36% vs. 13%), proteinuria (19% vs. 0%) and anemia (5% vs. 3%).

Patient (pt) baseline in the SANET-ep study included a majority of pts previously treated w/ chemo (~40%), somatostatin (27-35%), and everolimus (8%-12%) and we expect use in 2L pt, thru data supports use both 1/2L pts.

In Jun 2021, China CDE further approved surufatinib's NDA for the indication of NET-p. The sNDA was based on the SANET-p, a ph3 pivotal study (NCT02589821, N=195) in pts w/ advanced NET-p in China. The study met the pre-defined primary endpoint of PFS at a pre-planned interim analysis and was stopped early. Per ESMO 2020 and The Lancet Oncology (Sep 2020), mPFS was significantly longer for pts treated with surufatinib than in placebo group (10.9mo vs. 3.7mo, HR 0.491; 95% CI: 0.391-0.755; p=0.0011). The safety profile of surufatinib was manageable and consistent with observations in prior studies. Treatment was well tolerated for most pts, with discontinuation rates as a result of TEAEs of 10.6% in the surufatinib group as compared to 6.8% in placebo group.

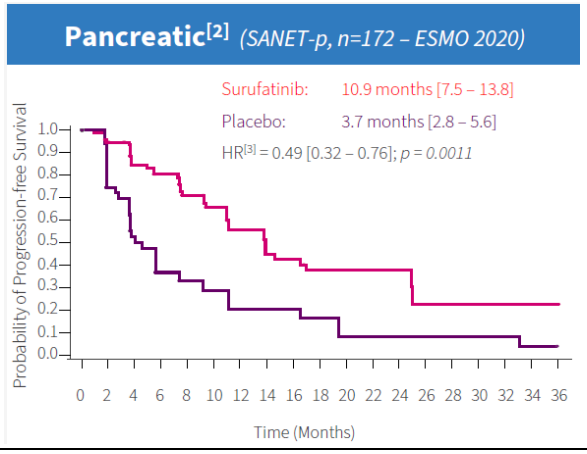
Frost & Sullivan estimated 67.6k newly diagnosed NET patients in China in 2020 and as many as 300k patients currently living with the disease based on the current incidence to prevalence ratio.

Figure 40: SANET-ep ph3 data met endpoint



Source: Company data

Figure 41: SANET-p ph3 study met endpoint



Source: Company data

Surufatinib / PD-1 inhibitor combinations in NEC/NET and GC/GEJ

Co. is conducting surufatinib + PD-1 combo studies w/ various PD-1 inhibitors (i.e. Junshi's toripalimab, Innovent's sintilimab, BeiGene's tislelizumab) across a variety of advanced solid tumors.

Figure 42: Co.'s ongoing Fruquintinib + PD-1 combo studies

Combo	Indication	Location	Stage	Enrollment (n)	Status (start yr)	NCT
Suru + toripali	NEN, BTC, GC, Thyroid cancer, SCLC, STS, EC, ESCC, NSCLC	China	Ph2	~250	Ongoing (2019)	NCT04169672
Frqu + sintili	Solid tumors	China	Ph1	95	Ongoing (2020)	NCT04427774
Frqu + tisleli	Solid tumors	US/EU	Ph1/2	120	Ongoing (2021)	NCT04579757

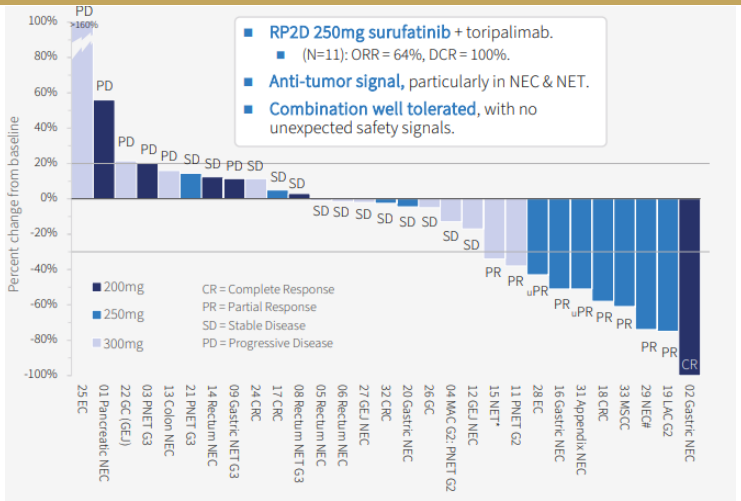
Sources: Company date, clinicaltrials.gov, CMS (HK)

In AACR 2020, Co. presented ph1 dose-finding study for surufatinib + toripalimab combo for patients (N=30) with various advanced solid tumors types, including NET G1-3, NEC, CRC, GC, ESCC and sq-cell carcinoma. In the RP2D surufatinib (250mg) + toripalimab cohort (N=11), the results showed an ORR of 64% and DCR of 100% (esp. in NEC & NET) good efficacy data with no unexpected safety signals. The positive anti-tumor signal indicates surufatinib has potential synergistic effect with PD-1 inhibitor.

In ASCO 2021, Co. presented positive ph2 trial results for patients with 2L NEC (NCT04169672, N=21) and 2L GC/GEJ (NCT04169672, N=21). Among 20 tumor evaluable patients in 2L NEC cohort, the results showed 20% ORR and 70% DCR, with 3.94mo mPFS. Among 15 evaluable patients in 2L GC/GEJ cohort, the results showed the confirmed and unconfirmed ORR were 13.3%/33.3%, respectively. The disease control rate (DCR) was 73.3% per RECIST v1.1 with 3.71mo mPFS. Despite one patient died due to unknown reasons in the 2L GC/GEC cohort, researchers believed surufatinib plus toripalimab showed manageable safety profile in both cohorts. We expect more data readout from the below suru+PD-1 combo trials in 2H21E/22E.

HCM also initiated a global trial of surufatinib + tislelizumab across a variety of advanced solid tumors. Co. expects the collaboration to maximize surufatinib's global value creation. Co. confirmed the study has enrolled first patient in Mar 2021.

Figure 43: Data of surufatinib + toripalimab Ph1 combo study in AACR 2020



Source: Company data

Figure 44: Suru + toripali Ph1 combo study ASCO 2021

Trial design			
Study ID		2019-012-00CH1	
Study Phase		Phase 2	
Treatment		Suru + Toripali	
Indication	**2L NEC**	**2L GC/GEJ**	**2L BTC**
Evaluable patient	20	15	39
Efficacy data			
mPFS (month)	3.9	3.7	3.7
mOS (month)	NR	NR	6.9
ORR (%)	20	13.3	n.a.
DCR (%)	70%	73%	n.a.
Safety profile			
AEs (%)	n.a.	n.a.	n.a.
Administrative Info			
NCT Number	NCT04169672	NCT04169672	NCT02966821
Data Source	ASCO 2021	ASCO 2021	ASCO 2021

Source: Company data

Surufatinib in other solid tumors

HCM is also enrolling patients in a Ph2b/3 study in 2L BTC in China Ex-China, a Phase 1b/2 study of surufatinib in PNET and BTC are ongoing with enrollment complete in NET. The company plans to initiate a Phase 3 study for US/EU registration in mid-2020.

Competitive landscape

In ep-NET/p-NET, the current standard of care is chemotherapy, somatostatin analog, or targeted therapy depending on location of NET. The competitive targeted therapy includes everolimus (mTOR inhibitor), sunitinib (VEGFR/PDGFR/KIT/RET inhibitor), and surufatinib (VEGFR 1/2/3/FGFR1/CSF-1R inhibitor). According to Guidelines for the Diagnosis and Treatment of Pancreatic Neuroendocrine Tumors in China (2020), surufatinib is of comparable efficacy among targeted therapy class with same 1A, grade I recommendation as an expected new treatment option for patients with advanced pNET. Of note, the guidelines highlighted the safety concerns for everolimus and sunitinib. We believe this could properly set surufatinib apart from its targeted therapy competitors. We summarize the efficacy data below. Note that studies of sunitinib and everolimus had comparable baseline patient characteristics vs. SANET-ep/SANET-p with regard to prior therapy (i.e. chemo, somatostatin analog).

Figure 45: Summary of available therapies in NET

	Octreotide	**Sunitinib**	**Lanreotide**				**Everolimus**		**Lu-Dotatate**	**Suru (vs PbO)**	
MoA	Somato statin analogue	VEGFR/PDGFR/KIT/RET	Somatostatin analogue				mTOR		SSTR binding (radiothera)	VEGFR 1/2/3/FGFR1/CSF-1R	
Drug admin.	Injection	Oral	Injection				Oral	Oral	Injection	Oral	Oral
Approval year	1998	2011	2007				2009	2011	2009	2020	2021
Trail design											
Study	PROMID	SUN 1111	CLARINET				RADIANT-3	RADIANT-4	NETTER-1	SANET-ep	SANET-p
Indication	NET (naive)	NET-p	Midgut NET	NET-p	Hindgut NET	NET-ep	NET-ep	NET	NET	NET-ep	NET-p
Disease Site	Small bowel	Pancreas only	All GI tract, pancreas				GI tract/pancreas/ lung/others		Small bowel	Almost all tracts (GI/pac./lung/other)	
Histology	Well Diff.	Well Diff.	Well or Moderately Diff.				Well or Moderately Diff.		Well Diff.	**Poorly Diff.**	
Disease status	Treat naive	Progressed past 12 mo	Stable disease				Progressed past 6 mo		Progressed past 3 yr	Progressed past 12 mo	
Enrollment (n)	85	171	33	42	11	205	205	410	116	198	172
Efficacy											
PFS (mo)	n.a.	12.6	61.5	29.7	55.0	11.0	11.0	11.0	40.0	10.9 (vs 3.7)	9.2 (vs 3.8)
OS (mo)	NR	38.6	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	NR	NR	NR
Admin info											
NCT	NCT 00171873	NCT 02589821	NCT 00353496				NCT 00510068	NCT 01524783	NCT 00510068	NCT02588170 NCT02589821	
Source	FDA	FDA	FDA				FDA	FDA	FDA	Company, Lancet	

Sources: Company data, FDA, PbO: Placebo; Note: Well differentiated NET patients have much longer OS (typically ~10 yrs or longer) than poorly differentiated (less than 1yr)

CMS estimates

We model for surufatinib sales in ep-NET/p-NET (China, US), 2L BTC and other indications based on the current approvals and ongoing clinical development.

ep-NET/p-NET (100% POS China / 80% POS ex-China): We model for peak penetration of 14% in in China, 9mo duration of therapy, assume USD42mn unadjusted in-market peak sales. Ex-China we estimate peak penetration of 6% and assume USD11.7k for monthly US net pricing at peak which equates to USD688mn in unadjusted peak sales.

2L BTC (85% POS China / 45% POS ex-China): We assume peak penetration to reach 9% market share of 2L BTC in China and assume 3.7mo duration of therapy. This yields USD34mn in unadjusted peak sales in China. We model peak penetration to reach 6% market share of 2L BTC in ex-China with USD36mn in unadjusted peak sales in China.

2L GC/GEJ in combination with PD-1 inhibitor (40% POS China / 10% POS ex-China): We assume peak penetration to reach 5%/6% market share of 2L GC/GEJ in China/ex-China and assume ~4mo duration of therapy, which equates to USD41mn/327mn in unadjusted peak sales in China/ex-China.

A comprehensive early-stage pipeline to watch

In addition to Co.'s late-stage assets, we see some promise for HCM's in-house early-stage candidates (i.e. HMPL-689, HMPL-523, HMPL-A83, etc.). We advise investors to continue to watch closely for additional details on these candidates from 2021 onwards.

Figure 46: Co.'s early stage drug candidates

Treatment	Indication	Target patient	Phase	Locations	Dose finding/safety	POC	Registration
HMPL-689 PI3Kδ	n.a.	Healthy volunteers	Ph1	Australia			
	iNHL		Ph1b	US/EU	To confirm reg. path in YE21E		
	FL/MZL		Ph2	China	NDA submission in YE22E/23E		
	MCL/DLBCL		Ph1b	China			
	CLL/SLL/HL		Ph1b	China			
HMPL-523 Syk	iNHL		Ph1b	US/EU/AUS	Data at conference YE21E		
	B-cell malignancies		Ph1b	China			
	ITP		Ph1b	China	Data at conference YE21E		
	AIHA		Ph2	China			
HMPL-453 FGFR1/2/3	IHCC		Ph2	China			
HMPL-306 FGFR1/2/3	Hemato tumors		Ph1	China			
	Hemato/ST tumors		Ph1	US/EU			
HMPL-295 (ERK, MAPK path)	ST tumors		Ph1b	China			
HMPL-760 3rd Gen BTK	Hemato tumors		IND	US/EU			
	Hemato tumors		IND	China			

Global China

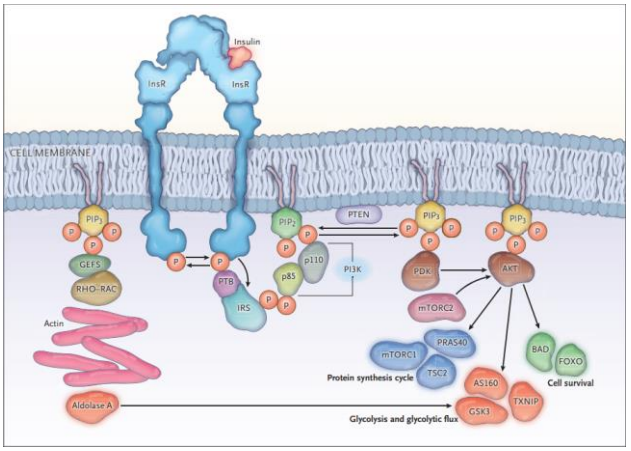
Source: Company data; Note: POC: proof-of-concept, iNHL: indolent non-Hodgkin lymphoma, FL/MZL: follicular lymphoma/marginal zone lymphoma, MCL: mantle cell lymphoma, DLBCL: diffuse large B cell lymphoma, CLL/SLL: chronic lymphocytic leukemia/small lymphocytic lymphoma, HL: Hodgkin's lymphoma, ITP: immune thrombocytopenia, AIHA: autoimmune hemolytic anemia, IHCC: intrahepatic cholangiocarcinoma, Hemato: hematological, ST: solid tumors, AUS: Australia

HMPL-689 (PI3Kδ inhibitor)

HMPL-689 is in-house developed PI3Kδ inhibitor. Phosphatidylinositol-3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) signaling is one of the most important intracellular pathways to the plasma membrane. The PI3K pathway is among the most frequently activated in human cancers, impacting almost 50% of the malignancies. Class IA isoforms PI3Kα, PI3Kβ and PI3Kδ are particularly strongly associated with cancer. PIK3CA (phosphatidylinositol 3-kinase, catalytic, α-polypeptide), the gene encoding the p110α subunit, are frequently mutated or amplified in the most common human cancers, such as breast cancers, colon cancer, gastric cancer, cervical cancer, prostate cancer, and lung cancer.

F&S expects the global PI3Ki global market will grow at 73.3% CAGR to RMB3.6bn in 2020E-25E, and 22.9% CAGR to RMB10.1bn in 2025E-30E, driven by the 1) expected label expansions into solid tumors and 2) broader adoption by oncologists.

Figure 47: The overview of PI3K/AKT/mTOR signaling pathway



Source: The New England Journal of Medicine

Clinical data by indication

Co. is currently conducting NDA enabling Ph2 trial with indications of follicular lymphoma (FL) as well as marginal zone lymphoma (MZL) in China. Company is expected to conduct regulatory dialogues w/ China CDE by YE21E. Co. expects to initiate the global Ph1 trial in the US, the EU and in Australia with indications of non-Hodgkin lymphoma (NHL). Co. expects the product to lose marketing exclusivity (LOE) in 2040E.

Figure 48: HMPL-689 (PI3Kδ) ex-China trial summary

Treatment	Indication	Target patient	Phase	Locations	Dose finding/safety	POC	Registration
HMPL-689		Healthy volunteers	Ph1	Australia			
HMPL-689	iNHL		Ph1b	US/EU	To confirm reg. path in YE21E		

Source: Company data; Note: iNHL: indolent non-Hodgkin lymphoma

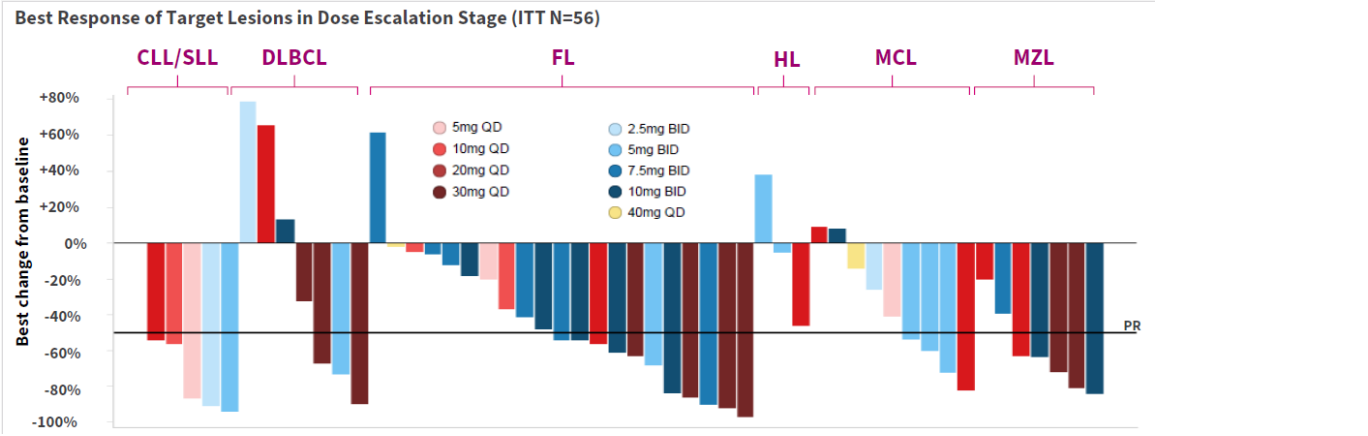
Figure 49: HMPL-689 (PI3Kδ) China trial summary

Treatment	Indication	Target patient	Study name (Phase)	Locations	Dose finding/safety	POC	Registration
HMPL-689	FL/MZL		Ph2	China	NDA submission in YE22E/23E		
HMPL-689	MCL/DLBCL		Ph1b	China			
HMPL-689	CLL/SLL/HL		Ph1b	China			

Source: Company data; Note: 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 lymphoma

In ASH 2020, HCM presented the ph1 dose escalation study (N=56) of HMPL-689. The result showed 52.9% ORR (o/w 11.7% CR) in efficacy evaluable patients (N=51). The duration of response (DOR) was 6.4 months (0.7-NR). One patient with FL who achieved CR (per post hoc independent radiologic review) was on treatment > 586 days. Regarding safety profile, the most common Grade ≥3 non-hematologic treatment emergent adverse events (TEAEs) were pneumonia and hypertension. Grade ≥3 hematologic TEAEs were neutropenia. No Grade 5 TEAE was reported.

Figure 50: Dose escalation data of HMPL-689 in ASH 2020



Sources: Company data, ASH2020

Based on the positive ph1 data in ASH 2020, Co. has initiated China registration intent ph2 trial for FL and MZL, with a primary efficacy endpoint of IRC-assessed ORR. Co. targets to complete the full enrollment targets for FL by 1H22E and for MZL by 2H22E. In addition, Co. expects to engage FDA in 2H21E through end of U.S. & EU ph1 meeting to confirm subsequent registrational path.

Competitive landscape

PI3K inhibitors are subdivided into dual PI3K/mTOR inhibitors, pan-PI3K inhibitors and isoform-specific inhibitors. Isoform-selective PI3K inhibitors has demonstrated improved specificity and reduced toxicity over dual PI3K/mTOR and pan-PI3K inhibitors, evidenced by several clinical trials for both solid and hematological malignancies. However, clinical trials on PI3Ki monotherapy have shown limited clinical activity, possibly due to acquired resistance and poor tolerability. As per Yang et al (Molecular Cancer 2019), the efficacy of PI3K inhibitors is limited for their narrow therapeutic window and frequent treatment-related toxicities, hypothesizing the agents are more likely to be optimally used in combination with other therapeutic modalities. As per Niu et al (J Pharmacol Exp Ther 2020), the liver toxicities observed with the first-generation PI3Kd inhibitors idelalisib, duvelisib, and dezapelisib (INCB040093) are caused by off-target effects that can be linked to this class of molecules.

Second-generation PI3Kδ inhibitor under development might overcome certain toxicity and tolerability issues associated with first-generation PI3Kδ inhibitor. Co. believe HMPL-689 has potentially better safety profile over approved PI3K inhibitors class, supported by 1) improved isoform selectivity which spares the PI3Kγ and PI3Kα isoforms, 2) better drug potency at whole blood level which reduce the compound related toxicity, and 3) improved pharmacokinetics (PK) characteristics, including CYP inhibition/induction which are important for avoid potential drug-drug interactions (i.e. under combo therapies).

Figure 51: Selectivity comparisons with approved PI3K drugs

EnzymeIC50 (nM)	HMPL-689	Idelalisib	Duvelisib	Copanlisib
PI3Kδ	0.8	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 **(142x)**	104 **(52x)**	2 **(2x)**	6.4 **(9x)**
PI3Kα (fold vs. PI3Kδ)	>1,000 **(>1,250x)**	866**(433x)**	143**(143x)**	0.5 **(1x)**
PI3Kβ (fold vs. PI3Kδ)	87 **(109x)**	293**(147x)**	8**(8x)**	3.7 **(5x)**
PI3Kδ human whole bloodCD63+	3	14	15	n/a

Source: Company data

Figure 52: Safety comparisons of PI3K drug class (all AEs / ≥G3 AEs, %)

	HMPL-689	Idelalisib	Copan-lisib	Duvelisib	Umbra-lisib	Parsac-lisib	Parsac-lisib	Zandelisib
Patient (n)	56	146	168	442	221	72	100	30
Neutropenia (%)	43/11	53/25	32/25	34/30	33/16	44/20	13/9	45/13
Anemia (%)	16/0	28/2	n.a.	20/11	27/3	31/8	14/5	13/0
Thrombocytopenia (%)	11/0	26/6	22/8	17/10	26/4	35/10	n.a.	22/0
Diarrhea/colitis (%)	<5/<5	47/14	36/5	50/23	58/10	36/9	44/11	45/19
Rash (%)	11/5	21/3	15/2	31/9	18/3	31/6	17/2	42/13
ALT increased (%)	27/2	50/19	n.a.	40/8	33/8	28/1	26/4	39/6
AST increased (%)	21/2	41/12	n.a.	37/6	32/7	29/1	19/2	25/6
Pyrexia (%)	14/0	28/2	n.a.	26/2	n.a.	18/1	13/1	n.a.
Pneumonia (%)	25/16	n.a.	21/14	21/15	PJP prophy.	n.a.	7% PJP prophy.	n.a.
Hypertension (%)	7/5	n.a.	35/27	n.a.	n.a.	7/0	n.a.	n.a.
Hyperglycemia (%)	11/2	n.a.	54/39	n.a.	n.a.	10/1	n.a.	n.a.

Source: Company data,

Figure 53 Global PI3K pathway trials data comparison (approved drugs)

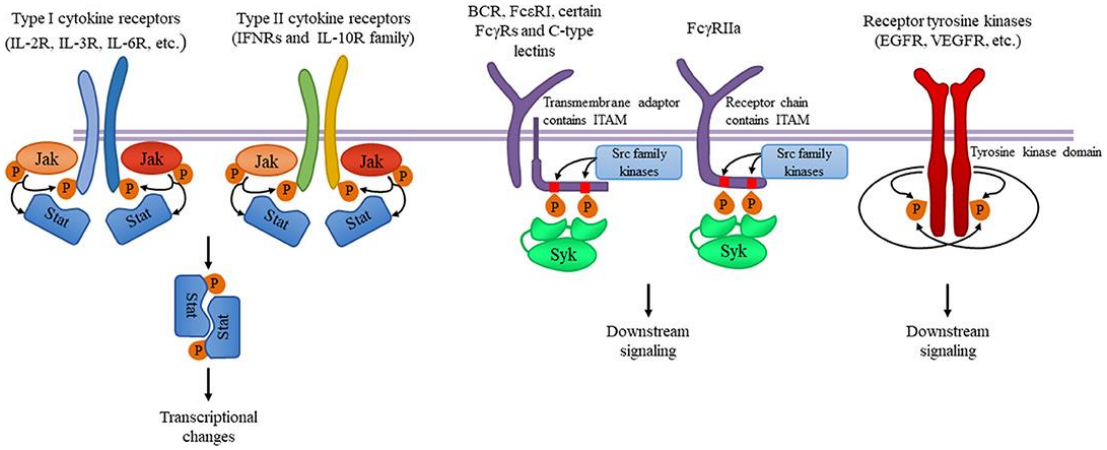
Company	Gilead	Gilead	Gilead	Gilead	Bayer	Novartis	Scura Bio/CSPC	Scura Bio/CSPC	TG Therapeutics
Generic name	**Idelalisib**	**Idelalisib**	**Idelalisib**	**Idelalisib**	**Copanlisib**	**Alpelisib**	**Duvelisib**	**Duvelisib**	**Umbralisib**
MoA	PI3Kδ	PI3Kδ	PI3Kδ	PI3Kδ	PI3Kα/PI3Kδ	PI3Kα	PI3Kδ/PI3Kγ	PI3Kδ/PI3Kγ	PI3Kδ/CK-1ε
Indication	2L r/r CLL	2L r/r FL	2L r/r SLL	1L r/r CLL	3L r/r FL	2L HR+/HER2- BC	3L r/r CLL/SLL	2l r/r FL	2L MZL/3L FL (r/r)
	-approved	- COND approval	- COND approval	Termina. Due to AEs	- COND approval	-approved	-approved	- COND approval	-approved
Study Phase	Phase 3	Phase 2	Phase 2	Phase 3	Phase 2	Phase 3	Phase 3	Phase 2	Phase 2b
Allocation	Randomized	Non-randomized	Non-randomized	Randomized	Non-randomized	Randomized	Randomized	Non-randomized	Non-randomized
Intervention Model	Parallel	Single	Single	Parallel	Single	Parallel	Parallel	Single	Single
Study Arms (vs. Placebo/SOC)	Idela+Ritux (vs PbO+Ritux)	Idela	Idela	Idela+Ritux+Bend (vs PbO+Ritux+Bend)	Copa	Alpeli+Fulve (vs PbO+Fulve)	Duveli (vs Ofatumu)	Duveli	Umbra
(n=evaluable pts/sample size)	(n=220)	(n=72/125)	(n=26/125)	(n=311)	(n=104/142)	(n=572)	(n=319)	(n=83/129)	(n=84/208)
Efficacy data									
Primary Outcome									
mPFS (month)	19.4 (vs. 6.5)	n.a.	n.a.	n.a.	12.5	11.0 (vs. 5.7)	13.3 (vs. 9.9)	n.a.	NR
HR	0.15	n.a.	n.a.	n.a.	n.a.	0.65	0.52	n.a.	n.a.
mOS (month)	n.a.	n.a.	n.a.	n.a.	42.6	n.a.	n.a.	n.a.	n.a.
HR	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
P-Value	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Secondary Outcome									
ORR (%)	92 (vs. 17)	54	58	n.a.	59	35.7 (vs. 16.2)	73.8 (vs. 45.3)	42	49 (MZL)/43 (FL)
mDOR (month)	NR (vs. 6.2)	NR	11.9	n.a.	14.1	n.a.	n.a.	n.a.	NR (MZL)/11.1 (FL)
Selected Dose	150mg BID	150mg BID	150mg BID	150mg BID	60mg Q1W (IV)	300mg QD	25mg BID	25mg BID	800mg QD
MTD (Dose Esca.)	350mg BID	350mg BID	350mg BID	350mg BID	0.8mg/kg Q1W (IV)				1800mg QD & NR
Safety profile									
AEs (%)	SAEs: 59.1 (vs. 39.8)	SAEs: 57.6	SAEs: 57.6	SAEs: 72.4 (vs. 44.2)	SAEs: 55.6	SAEs: 34.9 (vs. 16.7)	SAEs: 72.8 (vs. 32.3)	≥G3 88.4	SAEs: <20
Box Warning	x 5	x 5	x 5	x 5	No	No	x 4	x 4	No
Administrative Info									
NCT Number	NCT01539512	NCT01282424	NCT01282424	NCT01980888	NCT01660451	NCT02437318	NCT02004522	NCT01882803	NCT02793583
Study ID	Study 312-0116	Study 101-09 FL Cohort	Study 101-09 SLL Cohort	Study 312-0123	CHRONOS-1 FL Cohort	SOLAR-1	DUO	DYNAMO	UNITY-NHL MZL/FL Cohort
Data Source	FDA	FDA	FDA	Company	FDA	FDA	ASH 2018	FDA/ASCO 2019	AACR19

Sources: ASCO, ESMO, AACR, Company data, Evaluate, CMS (HK)

HMPL-523 (Syk) in hematological cancer and immune thrombocytopenia (ITP)

Syk (spleen tyrosine kinase) is a tyrosine kinase mainly expressed in hematopoietic cells and plays a critical role in regulating the B-cell signaling pathway in the upstream above PI3K and BTK tyrosine kinase.

Figure 54: An illustration of the mechanisms of action of Syk



Source: Frontiers

Co. believes its HMPL-523 has BIC potential to treat both hematological oncology and ITP (an autoimmune disease) as most early Syk inhibitors had shown high toxicity due to poor selectivity (i.e. fostamatinib, FDA approved ITP indication in 2018) or PK/PD properties (i.e. entospletinib, good efficacy but PK/PD).

Oncology indication: fostamatinib's oncology trials were halted due to off-target toxicities. In addition, fostamatinib, as a prodrug, has poor bioavailability and inconsistent drug metabolism in different patients. Entospletinib has shown good efficacy in treating CLL patients who were PI3K/BTK refractory. However, it has inconsistent drug exposures and risk of drug interaction (inhibition of CYP3A4/CYP2D6/CYP1A2 enzymes) in combo therapies. Gilead had dropped the development of entospletinib and sold it to Kronos Bio in 2020.

Co. has completed the Ph1 dose escalation study for indication of relapsed/refractory hematological malignancies. The study design has dosing range of 100-1000mg QD and 200-400m BID. The Ph1b dose expansion study is underway in ~30 clinical sites in both Australia (n=25) and China (190). Recommended Phase 2 dose was set at 600mg QD. The above Ph1/1b will be the basis for China registrational trials design. In addition, a peer company's Syk/JAK inhibitor, cerdulatinib has shown high ORR (76%) in FL when combined w/ rituximab. Therefore, we think HMPL-523 as a highly selectively Syk inhibitor also has combo potentials w/ biologics.

Figure 55: HMPL-523 ongoing studies and peers' Syk candidates (hematological indications)

Candidate	HMPL-523	HMPL-523	Fostamatinib	Entospletinib	TAK-659	Cerdulatinib	Cerdula+rituxi
Indication	iNHL	B-cell maligna.	DLBCL	CLL (prior PI3K/BTK)	r/r DLBCL	FL	FL
Study phase	Ph1b	Ph1/1b	Ph2	Ph2	Ph2	Ph2a	Ph2a
Enrollment (n)	~80	~200	101	18 (CLL cohort)	49	42	21
Allocation	Non-random.	Non-random.	Non-random.	Non-random.	Non-random.	Non-random.	Non-random.
Efficacy data							
mPFS (month)	n.a.	n.a.	n.a.	13.8	n.a.	n.a.	n.a.
ORR (%)	n.a.	n.a.	22	61	16	48	68
Safety profile							
SAEs (%)	n.a.	n.a.	26 (200mg BID)	n.a.	14	n.a.	n.a.
Admin info							
NCT number	NCT02503033	NCT02857998	NCT01499303	NCT01799889.	NCT03123393	NCT01994382	n.a.
Data source	Company	Company	Company	ASH 2015	ASH 2019	ASH 2019	ASH 2019

Sources: Company, FDA, ASH

ITP indication: ITP prevalence in China/US was 210K/35K in 2020. Most treatment for ITP are symptomatic, which do not prevent the progression of the disease and may be intolerable/unacceptable to many patients (i.e. corticosteroids, immunoglobulin infusion or splenectomy). Syk inhibitors can mute the signal transduction of Fc-activating/B-cell receptor, and therefore mitigate the antibody-mediated phagocytosis of platelets and offer an alternative treatment to hormone therapy, biological product infusion and surgery. Fostamatinib is the first and only approved Syk inhibitor for indication of ITP.

HCM plans to present efficacy and safety data of Ph1b China study at a scientific conference in YE21E. Co. is also planning a Ph3 study in YE21E. Beyond ITP, Co. is planning to launch a Ph2 trial for indication of autoimmune hemolytic anemia (AIHA) in China.

Figure 56: HMPL-523 vs Syk peers in ITP

Candidate	HMPL-523	Fostamatinib (vs PbO)	
Indication	ITP	ITP (FDA approval based on below two trials)	
Study phase	Ph1/1b	Ph3	Ph3
Enrollment (n)	~60	76	74
Allocation	Non-randomized	Randomized	Randomized
Interven model	Single	Parallel	Parallel
Efficacy data			
Stable platelet ≥50K/μL by Wk 24(%)	n.a.	17.6 (vs 0.0)	18.0 (vs 4.2)
Stable platelet ≥50K/μL by Wk 12(%)	n.a.	21.6 (vs 0.0)	24.0 (vs 12.5)
Safety profile			
SAEs (%)	n.a.	~4	~4
Admin info			
Study name	2018-523-00CH1	FIT-1	FIT-2
NCT number	NCT03951623	NCT02076399	NCT02076412
Data source	Company	FDA	FDA

Sources: Company, FDA, Note: PbO: placebo

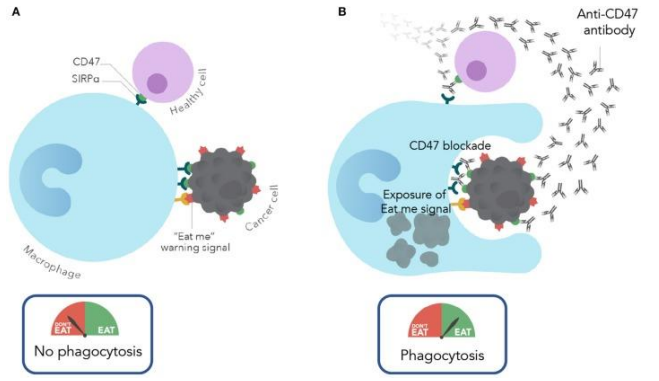
HMPL-A83 (CD-47 mAb) in solid tumors and hematological malignancies

HMPL-A83 is an IND stage αCD-47 mAb. CD47 functions as an innate and adaptive immune checkpoint, delivering the 'don't eat me' signals to signal-regulatory protein alpha (SIRPα) on macrophage then inhibiting phagocytosis. But the problem is that blocking CD47 can cause dangerous hematological side effects. The treatment-related hemolytic anemia is the major toxicity concern for potential CD47 targeting agents. CD47 was identified as a major homeostatic regulator of RBC turnover and a marker of self and protective mechanism against red blood cells (RBC) clearance. Thus, CD47 blockade has the potential to accelerate RBC clearance by unmasking of pro-phagocytic signals, leading to anemia when administered to patients. Thus, mitigating the on-target anemia observed with CD47 blockade is critical to successful clinical development of CD47 targeting agents.

Despite only a few anti-CD47 candidates in early clinical stage, immunotherapy targeting CD47/SIRPα pathway has been one investment hotspot. Following Gilead's USD4.9bn buyout of Forth Seven in Mar, AbbVie has also entered the CD47 race via a ~USD2bn of biodollars in-licensing deal with I-MAB in Sept in addition to lately Pfizer's initial investment in Trillium (an early stage CD47 pure player trading at mkt cap of ~USD1.0bn).

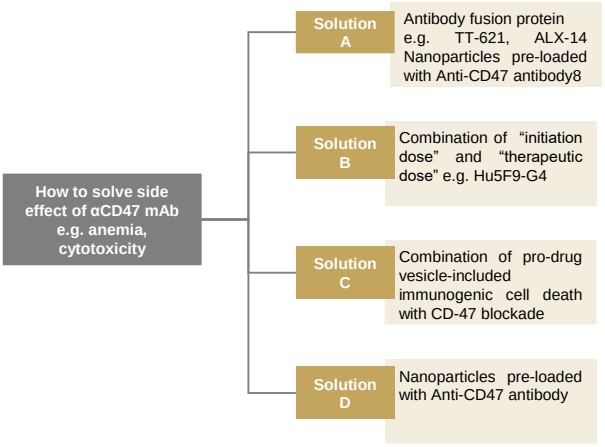
HCM founded HMPL-A83 is of high affinity and highly efficacious in animal tumor models, resulting in much reduced effect on RBC. Co. expects China and US IND submissions in YE21E. In the future, Co. is also looking into the potential combo possibilities w/ its HMPL-689 (PI3Kδ), HMPL-760 (BTK), and etc.

Figure 57: αCD47 pathway MoA overview



Source: Nature

Figure 58: Solutions to address αCD47 side effects



Source: Front. Immunol., 2020

We summarized several biological agents targeting CD47-SIRPα axis that have been developed for cancer treatment, including mAbs and recombinant proteins.

Figure 59: Global αCD47 pathway pipeline summary

Projects	Company	MoA	Indications	Stage
Magrolimab	Forty Seven/Gilead	CD47	MDS	Ph3
AO-176	Arch Oncology	CD47	Solid tumor (ST), r/r AML	Ph1/2
DSP107	KAHR Medical	SIRPα - 4-1BBL	Solid tumor	Ph1/2
Lemzoparlimab	I-MAB/AbbVie	CD47	ST, hematological tumor	Ph1/2a
OSE-172	OSE	CD47/SIRP-α	Solid tumor	Ph1/2
RRx-001	EpicentRx/SciClone	CD47/SIRP-α	Solid tumor	Ph1/2
Magrolimab	Forty Seven/Gilead	CD47	MDS	Ph1b
ALX148	ALX Oncology	CD47/SIRP-α	Gastric cancer	Ph1
IBI188	Innovent	CD47	AML	Ph1
TTI-621	Trillium	CD47/SIRP-α	Hematological tumor	Ph1
TTI-622	Trillium	CD47/SIRP-α	Hematological tumor	Ph1
TG-1801	TG Therapeutics	CD47xCD19	NHL	Ph1
IMM-01	ImmuneOnco	CD47	Hematological tumor	Ph1
IBI322	Innovent	CD47xPD-L1	MDS	Ph1
AK117	Akseo Bio	CD47/SIRP-α	ST, lymphoma	Ph1
CC-95251	Celgene	CD47/SIRP-α	ST, lymphoma	Ph1
FSI-189	Forty Seven/Gilead	CD47/SIRP-α	NHL	Ph1
IMC-002	ImmuneOncia	CD47	ST, lymphoma	Ph1
IMM-0306	ImmuneOnco	CD47xCD20	Lymphoma	Ph1
SHR-1603	Hengrui	CD47	Solid tumor	Ph1
SL-172154	Shattuck Labs	CD47xCD40	Overian cancer	Ph1
SRF231	Surface Oncology	CD47	ST, lymphoma	Ph1
TJ-C4GM	I-MAB	CD47-GM-CSF	n.a.	Ph1
TJ-L1C4	I-MAB	CD47xPD-L1	ST, lymphoma	Ph1
ZL-1201	Zai-Lab	CD47	Solid tumor	Ph1

Sources: Evaluate, CMS (HK)

Figure 60: Global αCD47 pathway candidates trials data comparison

Company	Forty Seven/Gilead	Forty Seven/Gilead	I-MAB/AbbVie	ALX Oncology	Innovent	Trillium	Trillium	TG Therapeutics	Akesobio	KAHR Medical
Drug name	**Magrolimab**	**Magrolimab**	**Lemzoparlimab**	**ALX148**	**IBI188**	**TTI-622**	**TTI-621**	**TG-1801**	**AK117**	**DSP107**
MoA	CD47	CD47	CD47	αCD47/SIRPα	CD47	CD47/SIRP-α	CD47/SIRP-α	CD47xCD19	CD47/SIRP-α	SIRPα - 4-1BBL
Indication	MDS	MDS	ST & Lymphoma	2L GC	AML	Lympho./Myeloma	ST & Lymphoma	Lymphoma	ST & Lymphoma	Solid Tumor (ST)
Study Phase	Phase 3	Phase 1b	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1/2
Allocation	Randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized
Intervention Model	Parallel	Single	Single	Single	Single	Single	Single	Single	Single	Single
Study Arms	Magro+Azaci (vs PbO+Azaci)	Magro+Azaci	Lemzo	ALX148+Trastu	IBI188	TTI-622+mAbs	TTI-621	TG1801+Ublitu	AK117	DSP107 /DSP107+Atezo
	(n=180)	(n=33)	(n=88)	(n=14)	(n=20)	(n=22)	(n=260)	(n=16)	(n=159)	(n=100)
Efficacy data										
ORR (%)	n.a.	91	n.a.	63.6	n.a.	~30	~20	n.a.	n.a.	n.a.
mDOR (month)	n.a.	NR	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Dose Escalation	n.a.	45mg/kg	30mg/kg	30mg/kg	30mg/kg	12mg/kg Ongoing	2mg/kg Ongoing	Ongoing	20mg/kg Ongoing	50mg/kg
Priming Dose	1mg/kg	1mg/kg	No Priming Dose	No Priming Dose	1-3mg/kg	n.a.	n.a.	n.a.	No Priming Dose	n.a.
Safety profile										
AEs (%)	n.a.	All Grade AEs	≥G3	≥G3	≥G3	≥G3	AEs	n.a.	≥G3	≥G3
	n.a.	68	n.a.	n.a.	n.a.	n.a.	No New Sig. Obers.	n.a.	n.a.	n.a.
G3 Anemia (%)	n.a.	17	No observed	7	5	4	n.a.	n.a.	No observed	n.a.
DLT	n.a.	n.a.	No DLT	No DLT	No DLT	One G4 DLT	One G3 DLT	n.a.	No DLT	No DLT
Hemoglobin Level. (%)	n.a.	n.a.	-10	n.a.	n.a.	Moderate platelet decrease	n.a.	n.a.	n.a.	-15
Administrative Info										
NCT Number	NCT04313881	NCT03248479	NCT03934814	NCT03013218	NCT03763149	NCT03530683	NCT02663518	NCT03804996	NCT04349969	NCT04440735
Study ID	5F9009	5F9005	TJ011133EDI101	ASPEN-01	CIBI188A102	TTI-622-01	TTI-621-01	TG-1801-101	AK117-101	DSP10-001
Data Source	Company	ASCO20	SITC20	SITC20	SITC20	ASH20	Company	EHA19	SITC20	Company

Sources: ASCO, ESMO, AACR, Company data, Evaluate, CMS (HK)

HMPL-453 (FGFR1/2/3) in cholangiocarcinoma

HMPL-453 is a highly selective FGFR 1/2/3 inhibitor for tumor growth and angiogenesis inhibitions. Co. is enrolling Ph2 study in 2L/2L+ IHCC patients w/ FGFR2 fusion. IHCC is the 2nd most common hepatic cancer after HCC. Around 10-15% IHCC pts has FGFR2 fusion. FDA approved single targeted FGFR inhibitors include erdafitinib (approved in 2019 for UC) and pemigatinib (approved in 2020 for IHCC).

Epitinib (EGFRm+) in glioblastoma

Co. has completed the Ph1/2 study of Epitinib and demonstrated ability to penetrate the blood-brain barrier. Glioblastoma pts typically has short overall survival period with a mOS of ~15 months in average and ~3 months in untreated pts. Co. is evaluating further development strategies for epitinib given 1) unmet clinical need and 2) shorted period required for mature OS data.

HMPL-306 (IDH1/2) in hematological malignancies and solid tumors

HMPL-306 has the potential of become the 1st dual inhibitor of IDH1 and IDH2. There are two approved IDHi: 1) ivosidenib (by Blueprint/CStone) and enasidenib (by Agois) for treatment of hematological cancers.

Co is conducting Phase 1 trial in China (since July 2020) in patients of r/r hematological malignancies with an IDH1 and/or IDH2 mutation. Co. expects to initiate a Phase 2 dose finding study in 2H21E.

HMPL-295 (ERK or MAPK pathway) in solid tumors

HMPL-295 is a highly selective small molecule inhibitor of ERK. ERK is at the downstream of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). Co is studying for the scientific and commercial potentials of this drug candidate for patients who have intrinsic or acquired drug resistance of upstream MAPK pathway. Currently there is no approved ERKi globally, though a few are under clinical studies (LY3214996 by Eli Lilly in Ph2, LTT462 by Novartis in Ph1, and BVD-523 by BioMed in Ph1).

HMPL-760 (BTK) in hematological malignancies

HMPL-760 is reversible, non-covalent, 3rd Gen BTK inhibitors. In vivo models shows it has higher drug potency against Ibrutinib. Currently, there four BTKi approved globally: 1) ibrutinb by AbbVie, 2) zanubrutinib by BeiGene, 3) acalabrutinib by AstraZeneca, and 4) orelabrutinib by InnoCare. Co. expects China and US IND submissions in 2H21E.

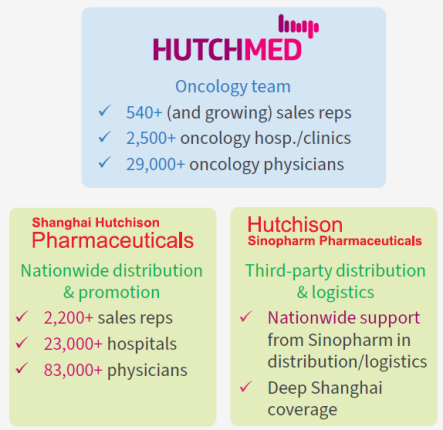
HMPL-653 (CSF-1R) in solid tumors

HMPL-653 is targeting CSF-1R driven tumors such as TGCT, histiocytic, and AML. It also has potential therapeutic value in solid tumors under adjuvant setting. Co. expects China IND submission in 3Q21E.

Proven Commercial Platform to support innovation

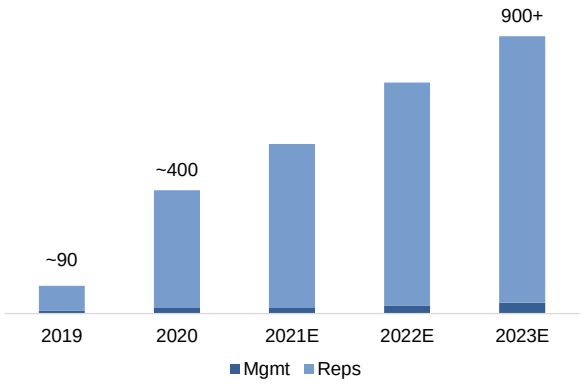
We believe HCM's Commercial Platform provides a steady cash flow and commercialization experience to support its efforts in more innovative therapeutic development. We anticipate that well-built platform will smoothen future commercial launches. HCM's commercial operation infrastructure mainly encompasses three arms, namely HCM in-house sales team and two joint ventures (Shanghai Hutchison Pharmaceuticals and Hutchison Sinopharm).

Figure 61: HCM commercial operations infrastructure



Source: Company data

Figure 62: HCM sales team expanding rapidly



Sources: Company data, CMS(HK)

HCM's oncology-focused in-house commercial team has expanded to 540+ sales reps in 1Q21, with a national coverage of 2,500+ hospital and 29,000 oncology physicians. The team has demonstrated strong capability to boost ELUNATE sales since HCM assumed commercial role in 4Q20 (HCM sales team recorded USD40.1mn in-market sales in 1Q 2021 vs. Eli Lilly sales team's USD23.5mn in total over Q1-Q3 2020). Co. targets to continue to scale up its sales team to 900+ staff in 2023E with SF productivity targeted to reach USD400k per sales reps.

Shanghai Hutchison Pharmaceuticals (SHPL) is jointly owned by HCM and Shanghai Pharmaceuticals (50%/50% stake), and is primarily engaged in the manufacture and sale of prescription drug products. The SHPL operation is large-scale, with a commercial team of about 2,300 staff managing the medical detailing and marketing of HCM's products not just in hospitals in provincial capitals and medium-sized cities, but also in the majority of county-level hospitals in China. SHPL's GMP-certified factory holds 74 drug product manufacturing licenses and is operated by about 520 manufacturing staff. SHPL's main product is She Xiang Bao Xin (SXBX) pill, an oral vasodilator prescription therapy for coronary artery disease. SXBX pill is the third largest botanical prescription drug in this indication in China, with market share of 18-19% nationally and ~50% in Shanghai.

Hutchison Sinopharm is a consolidated joint venture (51% stake) in collaboration with Sinopharm that provides logistics, marketing, and distribution for primarily prescription drugs manufactured by third parties. Hutchison Sinopharm has a dedicated team of over 120 commercial staff focused on two key areas of operation. Firstly, a commercial team that markets over 800 third-party prescription drug products directly to over 400 public and private hospitals in the Shanghai region and through a network of around 40 distributors to cover all other provinces in China. Second, a commercial team that markets Chi-Med's science-based infant nutrition products in over 8,000 outlets and through a network over 28,000 promoters and over 280,000 members.

In our view, HCM's well-established commercial platform yields an invaluable competitive advantage in distribution of its in-house innovative drugs currently in development. Further, we expect the company to leverage its existing infrastructure footprint to attract BD collaboration.

In addition, HCM is building up its U.S. sales team to support the potential launches of surufatinib in 2022E and fruquintinib in 2023E. We identify global capability will help to further add strength to HCM's commercial franchise.

Milestone and Catalyst Calendar

Figure 63: HCM: Milestone and Catalyst Calendar

Timeline		Product	Indication	Milestone / Event	Comment
2018					
Sep		Fruquintinib (VEGFR1/2/3)	3L mCRC	NDA approved by NMPA	Approval based on Ph3 FRESCO study (mOS: 9.3 vs 6.6 mos, HR: 0.65)
Nov		Fruquintinib	3L adv. NSCLC	Ph3 FALUCA trial results	Failed to meet the OS PE
Nov		Fruquintinib		Product launched	Product launched by Co. and Eli Lilly in China
2019					
Apr				Filed IPO app. to HKEX	Co.filed IPO app. to HKEX
Jun		Surufatinib (VEGFR/FGFRCSF-1R)	NET-ep	Met PE	Met PFS: Suru vs. PbO (mFPS: 9.2 vs 3.8 mos, HR: 0.33) in SANET-ep study
Jun				US IPO	To offer 12mn shrs at USD24/shr (ADS) on NASDAQ
Nov		Savolitinib (c-MET)	PRCC	SAVOIR trial terminated by AZ	SAVOIR trial, a Ph3 non-inferiority vs sunitinib was terminated earlier by AZ
Nov		Surufatinib	NET-ep	NDA accepted by NMPA	NDA accepted by on the SANET-ep study
Nov		Surufatinib	NET	FDA granted ODD	Suru. was granted with orphan drug designation (ODD) by FDA
Nov		Fruquintinib	3L mCRC	Entered NRDL20 via negotiation	Fruqu entered NRDL20 via nego. w/ -68% in ASP to RMB378/cap (5mg)
2020					
Jan		Surufatinib	NET-p	Met PE	Met PFS: Suru vs. PbO (mFPS: 10.9 vs 3.7 mos, HR: 0.49) in SANET-p study
Jan				US equity offering	To offer 4.4mn shrs at USD25/shr (ADS) on NASDAQ
Apr		Surufatinib	NET	FDA granted FTD	Suru. was granted fast track designation (FTD) & eligibe for US priority/rolling review
May		Fruquintinib + tislelizumab	Solid tumors	Entered collaboration w/ BeiGene	To enter global collaboration to evaluate the Suru+tislelizumab (PD-1) combo in STs
May		Savolitinib	Exon 14 NSCLC	NDA accepted by NMPA	NDA accepted base on Ph2 study for MET Exon 14 skipping mutation NSCLC
Jun		Fruquintinib	3L/3L+ mCRC	FDA granted FTD	Fruqu. was granted FTD for mCRC
Jun				US equity offering	To offer 4mn shrs at USD25/shr (ADS) thru PIPE, plus warrant (USD100mn underlying) to General Atlantic
Jul		Savolitinib	Exon 14 NSCLC	NMPA granted priority review	Priority review granted based on Ph2 study for MET Exon 14 Skipping mutation NSCLC
Jul		Fruquintinib		Collaboration agreement update	Co. resumed commericial responsibility from Eli Lilly, w/ latter raised royalties to 70%-80% on China sales
Aug		Surufatinib	NET	Plan to submit MAA to EMA	Co. to submit MAA to EMA within FY21 after meeting w/ CHMP
Sep		Surufatinib	NET-p	NDA accepted by NMPA	NDA accepted based on the SANET-p study
Sep		Surufatinib	NET-p	SANET-p readout at ESMO20	Co. published SANET-p study data at ESMO20
Nov				US equity offering	To offer ~3.3mn shrs at USD30/shr (ADS) or USD100mn thru PIPE to Canada Pension Plan (CPP)
Dec		HMPL-689 (PI3Kδ)	r/r Lymphoma	Ph1 data readout at ASH20	Co. to present HMPL-689's Ph1 data at ASH20
Dec				Shanghai factory ground breaking	Construction completion by FY25E (Ph1/Ph2 250mn/550mn tabs/yr), 5x of Suzhou capacity
Dec		Surufatinib	NET	Initiated US NDA submission	Co. initiated US NDA submission as part of the rolling review process
Dec		Surufatinib	NET-ep	NDA approved by NMPA	NDA approved based on Ph3 SANET-ep study
2021					
Jan				Partner w/ Inmagene in Immuno area	Co. out-licensed 4 pre-IND cadidates to Inmagene (upfront/comm. miles USD95mn/USD135mn, double digit royalties)
Jan		Savolitinib + targrisso	EGFRm MET+ NSCLC	Ph1b data readout WCLC	Co. to present Ph1b TATTON study part B and D (savo+targri) data at WCLC
Mar		Surufatinib + tislelizumab	adv. Solid tumors	Ph1b/2 study initiation	Studies initiated in the US & EU
Mar				Divestment of HBYS	To sell HBYS, a non-core business to GL Capital for USD169mn (22x PE, FY20)
Apr				US equity offering	To offer ~3.3mn shrs at USD30.5/shr (ADS) or USD100mn thru PIPE to Baring Private Equity Asia
May		Surufatinib	NET-ep/p	FDA rolling submission completed	FDA rolling submission completed
Jun		Fruqu/Suru/Savo		Data presentation at ASCO21	Co. presented mono/combo studies of savo/fruqu/suru
Jun		Surufatinib	NET-p	NDA approved by NMPA	NDA approved based on the SANET-p study
Jun		Savolitinib	Exon 14 NSCLC	NDA granted cond. approval	Cond. approval based on Ph2 study for MET Exon 14 Skipping mutation NSCLC
Jun				HK IPO pricing announced	Co. announced HK IPO pricing (104mn ordinary shrs at HKD40.1/shr, or HKD 4.17bn)
Jun				HK IPO debut	Co. started to trade on SEHK under ticker "13"
Jul		Surufatinib	NET-ep/p	NDA accepted by FDA	NDA accepted based on the SANET-ep/p study, PADUFA data set on Apr 30, 2022
Jul		Surufatinib	NET-ep/p	NDA MAA submitted to EMA	MAA submitted and validated by the EMA
2H21E		Savolitinib	EGFR-TKI ref MET+ NSCLC	Savo+targri study initiation	Savo+targri combo China study (SACHI) initiation
2H21E		Savolitinib	EGFR ref MET+ NSCLC	Savo+targri study initiation	Savo+targri combo China study (SANOVO) initiation
YE21E		Fruquintinib	PD-1 combo	Ph2 data readout	Ph2 data readout at a academic conference
YE21E		HMPL-689	2L FL/MZL	Data readout (CN)	Data readout at a academic conference
YE21E		HMPL-5232	ITP	Data readout (CN)	Data readout at a academic conference
2022					
Apr		Surufatinib	NET (non-panc./panc.)	PADUFA action date	PADUFA action date on Apr 30, 2030
1H22E		Savolitinib	2/3L EGFRm+ NSCLC	Topline data readout	Topline data publishing at a academic conference
2H22E		Fruquintinib	2L GC	Topline data readout	Topline data (FRUTIGA study) publishing at a academic conference
2022/2023					
2H22E/23E		Fruquintinib	3L/3L+ CRC	NDA filing in US/EU/Japan	Co. to file NDA for 3L/3L+ CRC in US/EU/Japan based on FRESCO-2 data
23E		Commercial development		900+ sales reps	Co.'s sales rep team to reach 900+ by YE23E

Source: Company data

Valuation Summary

We arrived at our SOTP-based TP using a risk adjusted NPV (rNPV) approach, with sensitivities on the peak sales and the probability of success (PoS) of various molecules. We detail below our assumption and valuation results.

Figure 64: rNPV-based SOTP valuation and main assumptions

(USD mn)	Target	R&D Status*	Partner	Major Indication	Launch date	Peak sales	PoS**	Rights	rNPV
Core portfolio drugs (rNPV)									**6,804**
Existing portfolio									
Surufatinib	VEGFR1/2/3, FGFR1&CSF-1R	Approved (CH), NDA (U.S.)	Junshi / Innovent / BeiGene	Neuroendocrine tumor (NET), biliary tract, thyroid, solid tumors (w/ I/O combo)	2021	1,093	100% (CH), 80% (U.S.)	100% (WW)	2,368
Fruquintinib	VEGFR1/2/3	Approved (CH), P2/3 (U.S.)	Eli Lilly / Innovent / Genor / BeiGene	CRC, GC, NSCLC, solid tumors (w/ I/O combo)	2018	1,062	100% (CH), 50% (U.S.)	70-80% sales (CH); 100% sales (WW)	946
Savolitinib	c-MET	Approved (CH), Reg. (U.S.)	AstraZeneca	NSCLC, RCC, GC CRC (w/ I/O combo)	2021	2,236	100% (CH), 70% (U.S.)	30% royalty (CH); 9-18% royalty (ex-CH)	2,443
R&D Pipeline									
HMPL-689	PI3Kδ	P1b/2	-	B-cell malignancies - indolent NHL	2025	289	40%	100% (WW)	434
HMPL-523	Syk	P1b/2	-	Cholangiocarcinoma	2025	240	40%	100% (WW)	365
HMPL-453	FGFR1/2/3	P2	-	Glioblastoma, HCC	2025	130	40%	100% (WW)	87
Epitinib	EGFRm+	P2	-	Hematological malignancies, solid tumor	2025	130	40%	100% (WW)	87
HMPL-306	IDH1/2	P1	-	Solid tumor	2025	130	20%	100% (WW)	44
HMPL-295	ERK(MAPK pathway)	P1	-	Solid tumor	2025	130	20%	100% (WW)	44
HMPL-653	CSF-1R	IND	-	Solid tumor	2026			100% (WW)	-
HMPL-A83 mAb	CD47.	IND	-	Solid tumor, hematological malignancies	2026			100% (WW)	-
HMPL-760	3rd Gen BTK	IND	-	Hematological malignancies	2026			100% (WW)	-
Non-core portfolio (10x 23E NOPAT)									**477**
Net cash									**424**
Valuation (USD mn)									**8,093**
No of shares (m)									849
Valuation per ADR share (USD)									**45.5**
Capital allocation premium									**20%**
TP (USD)									**54.6**

*Sources: Company data, CMS(HK), Notes1: CRC: colorectal cancer, GC: gastric cancer, NSCLC: non-small cell lung cancer, I/O: immuno-oncology, RCC: renal cell carcinoma, NHL: non-Nodgkin lymphoma, HCC: hepatocellular carcinoma; Notes2: *represents the lead indication of the molecule, **represents the highest PoS of indication of the molecule*

Price assumptions on major products

We present below the pricing estimates for HCM's three key molecules in China and ex-China market.

Figure 65: Our pricing estimates for Innovent's main molecules

Existing portfolio (USD mn)	Partner	Target	Indications	Region	Stage	Launch Yr	PoS	rNPV (USD mn)	Dosage Forms	Dosing frequency	mDOR (month)	ASP (RMB)	ASP (USD)	Annual Treatment cost (USD)	Monthly Treatment cost (USD)
Surufatinib						**2021**		**2,368**							
surufatinib		VEGFR1/2/3, FGFR1& CSF-1R	NET-ep/p	CN	Approved	2021	100%	432	50mg	300mg QD	8.40	32.32	4.97	7,518	895
surufatinib			2L BTC; chemo refactory	CN	NDA	2021	85%	50	50mg	300mg QD	3.73	32.32	4.97	3,341	895
surufatinib + PD-1	Junshi / Innovent		Solid tumor (NENs, ESCC, BTC; SCLC, GC, Sarcoma; TC, EMC, NSCLC)	CN	P2	2024	40%	58	50mg	300mg QD	3.73	32.32	4.97	3,341	895
surufatinib			NET	US/EU	NDA	2022	80%	1,692	50mg	300mg QD	8.40		70.00	105,840	12,600
surufatinib			BTC, Soft tissue sarcoma	US	P2	2025	45%	23	50mg	300mg QD	3.73		70.00	47,040	12,600
surufatinib + PD-1	BGNE		Solid tumor (2L GC)	US/EU/JP	IND	2026	10%	115	50mg	300mg QD	3.73		70.00	47,040	12,600
Fruquintinib						2018		**946**							
fruquintinib	Eli Lilly	VEGFR1/2/3	3L CRC	CN	Approved	2018	100%	188	5mg	5mg QD	6.53	264.60	40.71	5,984	916
fruquintinib + chemo	Eli Lilly		2L GC	CN	Reg	2022	50%	141	5mg	5mg QD	3.73	264.60	40.71	3,419	916
fruquintinib + PD-1	Eli Lilly / Innovent/Genor		CRC, EMC, RCC, HCC, CRC, NSCLC	CN	P2	2024	30%	84	5mg	5mg QD	6.53	264.60	40.71	5,984	916
fruquintinib			2L CRC	Global	P2/3	2024	50%	305	5mg	5mg QD	6.53		630.00	92,610	14,175
fruquintinib			BC	US	P2	2024	35%	159	5mg	5mg QD	5.60		630.00	79,380	14,175
fruquintinib + PD-1	BGNE		TNBC, solid tumor	US	IND	2025	10%	71	5mg	5mg QD	5.60		630.00	79,380	14,175
Savolitinib						2021		**2,443**							
savolitinib	AZ	c-MET	NSCLC MET exon14 skipping / MET+	CN	Approved	2021	100%	524	100mg	400mg QD	8.40	70.00	10.77	10,855	1,292
savo+TAGRISSO	AZ		2L NSCLC_EGFR TKI ref; MET+	CN	P3	2023	70%	167	100mg	300mg QD	7.00	70.00	10.77	6,785	969
savo+TAGRISSO	AZ		1L NSCLC Naïve MET+ & EGFRm	CN	P3	2023	70%	446	100mg	300mg QD	10.50	70.00	10.77	10,177	969
savolitinib	AZ		2L GC MET+	CN	P3	2023	60%	41	100mg	300mg QD	7.70	70.00	10.77	7,463	969
savo+TAGRISSO	AZ		2/3L NSCLC_EGFRm; Tagrisso ref.; MET+	Global	Reg	2023	70%	501	100mg	300mg QD	7.00		224.00	141,120	20,160
savo+IMFINZI	AZ		Papillary RCC_MET+/ALL	EU	Reg	2023	70%	147	100mg	300mg QD	7.00		224.00	141,120	20,160
savo+IMFINZI	AZ		Clear cell RCC_VEGFR TKI refractory	EU	P2	2024	40%	454	100mg	300mg QD	7.00		224.00	141,120	20,160
savolitinib	AZ		GC MET+	KR	P2	2024	40%	85	100mg	300mg QD	7.70		224.00	155,232	20,160
savolitinib	AZ		CRC MET+	US	P2	2024	40%	78	100mg	300mg QD	7.00		224.00	141,120	20,160

Source: CMS(HK) estimates

- We assume that surufatinib will be priced at USD895/mo (initially price assumption at USD1,119/mo post the anticipated addition to the 2021E NRDL) in China for peak sales periods (estimated in 2026E). We reckon the full treatment cost would actually vary across indications depending how long patients can stay on the course. In its main indications (ep-NET/p-NET), SANET-ep/-p ph3 study showed 9.2-10.9mo median duration of treatment (mDOT), while only 3.7-3.9mo mDOT in 2L BTC, 2L GC and 2L NET/NEC. We assume that surufatinib will be priced at USD12,600/mo in the U.S. for peak sales periods (2028E), which is ~30-40% discount to current sunitinib and afinitor pricing.
- We assume that fruquintinib will be priced at USD916/mo (30% discount to its 2019 NRDL price of USD1,308/mo or RMB378/per 5mg pill) in China for peak sales periods (estimated in 2026E). We reckon the full treatment cost would actually vary across indications depending how long patients can stay on the course. Despite Ph3 FRESCO study showed fruquintinib mono only yielded 4mo mDOT for 3L CRC, ASCO 2021 showed fruquintinib+PD-1 combo increased mDOT to 6.9-7.3mo. We assume that fruquintinib will be priced at USD14,175/mo in the U.S. for peak sales periods (2030E), which is ~40% discount to current Stivarga (Regorafenib) treatment cost.
- We assume that savolitinib will be priced at USD969-1,292/mo (initially price assumption at USD1,385-1,846/mo post the anticipated addition to the 2021E NRDL) in China for peak sales periods (estimated in 2025E). We reckon the full treatment cost would actually vary across indications depending how long patients can stay on the course. In its main indications (MET+ EGFR TKI refractory NSCLC), TATTON ph2 study showed diverse mDOT for MET+ 3rd gen. EGFR TKIref. (5.4mo) and MET+ 1st/2nd gen. EGFR TKIref. (9.0mo). We assume that savolitinib will be priced at USD20,160/mo in the U.S. for peak sales periods (2028E), in line with current tepotinib monthly treatment cost.

Probability of Success factor in our rNPV model

- This measures the probability of approvals in a certain indication. In general, we assume 15% likelihood of approval for a molecule in ph1, 30%-40% for ph2, and 60%-70% for ph3, 85% for BLA/NDA stage.
- In the case that the molecule received overseas approvals or demonstrated positive pivotal trial data, we use 10-15% probability for the drug in the preclinical to ph1 stage, 35%-45% for the drug in ph2, 70%-80% for the drug in ph3, and 90% for BLA/NDA stage, to reflect a bit higher likelihood of approval if same indication has approved in China.

Penetration factor in our rNPV model

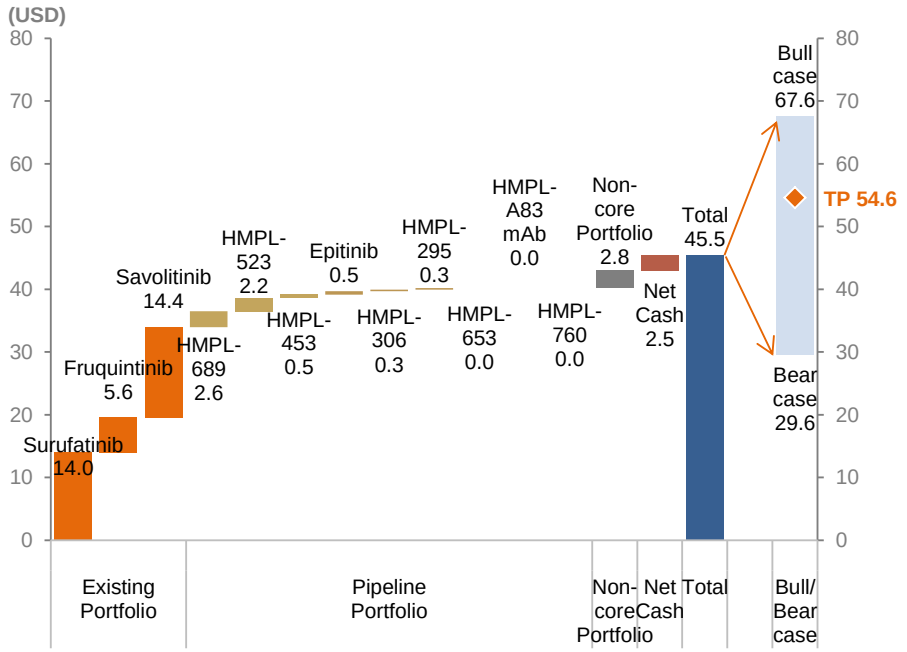
- This measures HCM's patient share in the addressable patient population in a certain indication. It is defined as the multiplication of the molecule penetration rate (the percentage of the addressable population being treated with this drug) and HCM's patient share.
- In general, the molecule penetration rate is 15-50% depending on its overseas approvals, pivotal trial data and competitive landscape.
- We also assume that HCM's patient share should be 15-50% depending on its order of entry into the market, the strength of collaboration with MNCs, and synergistic potential with its existing portfolio.

Other key assumptions and rationales:

- We assume 28-35% "normalized" FCF and NOPAT margin for innovative pipelines. The underlying assumption is that over long term, the maintenance CAPEX should equal to depreciation and amortization, and that the additional working capital investment should be miniscule.
- For non-core business, we assume the 5% sales CAGR as these businesses have entered mature phase.
- We apply 20% of capital allocation premium to the SOTP valuation to arrive at the equity value. This is because we reckon that HCM should have an enhanced global commercial platform and a well-capitalized financial position (~USD950mn cash resources as of Jun 30, 2021), which would allow it to pursue more M&A and licensing opportunities.

We present below sensitivity exercise for HCM. The main variables in our assumptions are the peak sales (+/-30% relative to our base case) in each marketed molecule, the probability of success (+/-30% relative to our base case) in each molecule in the pipeline.

Figure 66: HutchMed's SOTP and sensitivity analysis



Source: CMS (HK) estimates

Figure 67: WACC assumption

Cost of equity (%)	
Risk free rate (%)	3.3
Beta	0.8
Equity risk premium (%)	8.3
CAPM unleveraged discount rate	**9.9**
Cost of debt (%)	
Average spread over risk-free rate (%)	5.0
Pre-tax cost of debt (%)	8.3
Average corporate tax rate for company (%)	19.0
Post-tax cost of debt (%)	**6.7**
Estimated target gearing (net debt/EV) (%)	10.0
WACC (%)	**9.6**

Source: CMS (HK) estimates

For the HKEX shares of HCM, we assume the same SOTP valuation approach to arrive TP at HKD84.8/shr (given 1 ADS = 5 ordinary shares, USD/HKD FX rate assumed at 7.77).

Key risks

Clinical failure risk

Co. expects the SAVANNAH study (savo + targrisso combo) data to support a global Ph3 study initiation in 2H21E. Clinical failure would represent downside to our estimates and set back to HCM's efforts to expand outside of China.

Commercial execution risk:

Co. has a commercial focus in both China and US. These two markets each has unique market environment and requires different market access strategies. A worse than expected launch of any of pipelines would cause downside to our estimates/valuation.

Geopolitical risk:

Political uncertainty both with regard to internal and international dynamics could present headline and longer term risks to the investment case.

Collaboration risk

Co. has form a broad strategic collaboration with MNCs and domestic players. Poor collaboration would adversely affect Co.'s clincial and commercialization strategy.

Policy risk

NRDL reforms in China accelerated market access for innovative drugs. However, the expansion of NRDL comes with pressure on drug pricing. As such, there remains a downside price risk on commercial outlook for HCM's existing portfolio and its pipeline than our expected.

Financial summary

Revenue

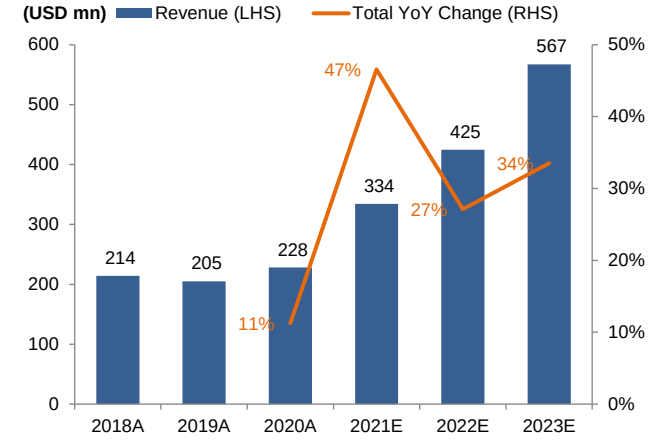
HCM recorded consolidated revenue of USD214mn/205mn/228mn in 2018-2020, primarily from 1) revenue from Oncology/Immunology of USD41mn/USD27/mn/USD30mn; and 2) revenue from its Other Ventures of USD173mn/178mn/198mn. We forecast consolidated revenue to grow at 38% CAGR to USD334mn/425mn/567mn over 2021E-23E, mainly driven by strong growth in Oncology/Immunology segments (+124% CAGR) and a steady mid-single digit growth of its Other Ventures.

Revenue from Oncology/Immunology primarily comprises 1) revenue from ELUNATE in China, consisting a) revenue from the sales of ELUNATE to Eli Lilly which HCM manufacture and sell at cost, b) promotion and marketing services to Eli Lilly and royalty revenue; and 2) revenue recognized under licensing, co-development and commercialization agreements for upfront, milestone and research and development services payments for its drug candidates developed in collaboration with AstraZeneca and Eli Lilly. We model revenue from Oncology/Immunology to grow at 124% CAGR to USD127mn/USD207mn/339mn over 2021E-23E, driven by fast sales uptake and milestone income of fruquintinib (ELUNATE), surufatinib (SULANDA) and savolitinib (ORPATHYS).

We model in-market sales of ELUNATE to grow to USD202mn in 2023E from USD34mn in 2020E, supported by proven HCM's oncology-focused in-house sales team to boost ELUNATE sales since HCM assumed commercial role in 4Q20 (HCM sales team recorded USD40.1mn in-market sales in 1Q 2021 vs. Eli Lilly sales team's USD23.5mn in total over Q1-Q3 2020). Additionally, we reckon newly launched products, SULANDA and ORPATHYS, to achieve fast sales uptake to USD119mn/219mn in 2023E, respectively.

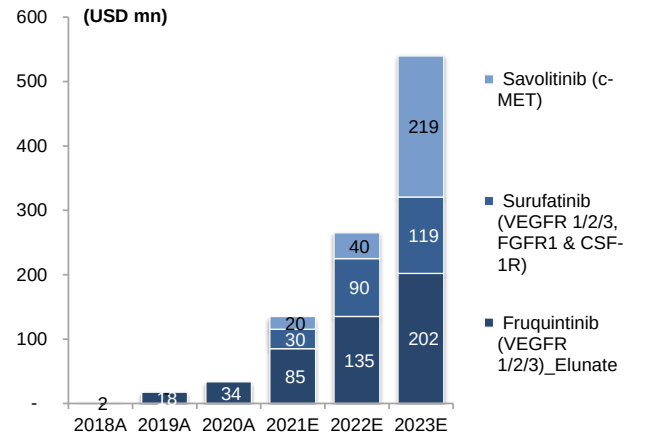
Revenue from Other Ventures primarily comprises revenue from prescription drugs including the commercial services, logistics and distribution business of our consolidated Hutchison Sinopharm joint venture with Sinopharm. We project revenue from Other Ventures to grow steadily at mid-single digit to USD207mn/217mn/228mn on the backdrop of a mature-phase portfolio and ongoing generic GPO impacts.

Figure 68: Total revenue and growth



Sources: Company, CMS (HK) estimates

Figure 69: In-market sales of products



Sources: Company, CMS (HK) estimates

Figure 70: In-market sales of HCM innovative drug products (USD mn)

In-market sales of products (USD mn)	2018A	2019A	2020A	2021E	2022E	2023E
Fruquintinib (VEGFR 1/2/3)_ELUNATE	2	18	34	85	135	202
Surufatinib (VEGFR 1/2/3, FGFR1 & CSF-1R)			-	30	90	119
Savolitinib (c-MET)			-	20	40	219
Total	**2**	**18**	**34**	**135**	**265**	**540**
Yoy growth (%)		*935%*	*91%*	*301%*	*96%*	*104%*

Sources: Company, CMS (HK) estimates

Figure 71: Revenue breakdown over 2018A-2023E

Revenue (USD mn)	2018A	2019A	2020A	2021E	2022E	2023E
Oncology/Immunology	**41**	**27**	**30**	**127**	**207**	**339**
Goods	**3**	**8**	**11**	**53**	**128**	**191**
Fruquintinib, (VEGFR 1/2/3) ELUNATE	3	8	11	21	34	50
Surufatinib (VEGFR 1/2/3, FGFR1 & CSF-1R)				30	90	119
Savolitinib (c-MET)				2	4	22
Services	**26**	**16**	**14**	**55**	**47**	**71**
Services - Commercialization – ELUNATE	-	-	4	30	47	71
Services - Collaboration R&D - third parties	18	16	10	25		
Services - R&D services - related parties	8	0	0			
Other collaboration revenue	**12**	**3**	**5**	**19**	**32**	**77**
Royalties - third parties	0	3	5	19	32	77
Fruquintinib (VEGFR 1/2/3)_ELUNATE	0	3	5	13	20	30
Savolitinib (c-MET)	-	-	-	6	12	47
Licensing - third parities	12	-	-			
Other Ventures	**173**	**178**	**198**	**207**	**217**	**228**
Goods - Third parties	153	168	192	202	212	223
Goods - Related parties	8	8	5	5	5	5
Services - Commercialization - third parties	12	3	-	-	-	-
Total	**214**	**205**	**228**	**334**	**425**	**567**
YoY growth (%)						
Oncology/Immunology	**-**	***(35)%***	***13%***	***319%***	***64%***	***64%***
Goods	**-**	***144%***	***40%***	***370%***	***140%***	***50%***
Fruquintinib, (VEGFR 1/2/3) ELUNATE	-	*144%*	*40%*	*88%*	*59%*	*50%*
Surufatinib (VEGFR 1/2/3, FGFR1 & CSF-1R)	-	-	-	-	*200%*	*32%*
Savolitinib (c-MET)	-	-	-	-	*100%*	*448%*
Services	**-**	***(37)%***	***(13)%***	***291%***	***(14)%***	***50%***
Services - Commercialization – ELUNATE	-	-	-	*697%*	*59%*	*50%*
Services - Collaboration R&D - third parties	-	*(12)%*	*(37)%*	*156%*	*n.a.*	-
Services - R&D services - related parties	-	*(94)%*	*(1)%*	*n.a.*	-	-
Other collaboration revenue	**-**	***(79)%***	***84%***	***283%***	***72%***	***140%***
Royalties - third parties	-	*916%*	*84%*	*283%*	*72%*	*140%*
Licensing - third parties	-	*(100)%*	-	-	-	-
Other Ventures	**-**	***3%***	***11%***	***5%***	***5%***	***5%***
Goods - Third parties	-	*10%*	*15%*	*5%*	*5%*	*5%*
Goods - Related parties	-	*(8)%*	*(28)%*	-	-	-
Services - Commercialization - third parties	-	*(78)%*	*n.a.*	-	-	-
Total	**-**	***(4)%***	***11%***	***47%***	***27%***	***34%***

Sources: Company, CMS (HK) estimates

Cost of Revenue and Gross Profit

HCM COGS of revenue are primarily attributable to the cost of revenues of Hutchison Sinopharm and Hutchison MediPharma. HCM cost of revenues to related parties is attributable to sales to indirect subsidiaries of CK Hutchison.

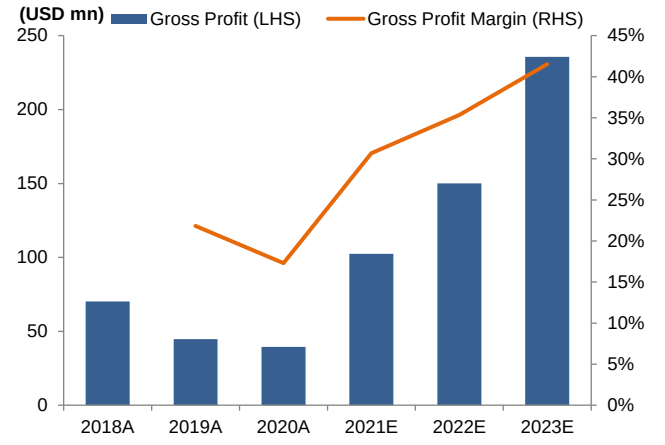
HCM gross profit margin declined from 33% to 17% over 2018-20, reflecting the change in revenue mix due to increased proportion of sales of lower margin products by Hutchison Sinopharm. With faster sales uptake and addition launch of its higher margin innovative drugs, we forecast an uptrend in gross margin from 31% to 42% in 2021E-2023E to reflect revenue mix shifting into Oncology/Immunology segments.

Figure 72: Gross profit and GPM breakdown over 2018A-2023E

Gross profit (USD mn)	**2018A**	**2019A**	**2020A**	**2021E**	**2022E**	**2023E**
Oncology/Immunology	**40**	**22**	**18**	**80**	**127**	**211**
Goods	**2**	**3**	**5**	**31**	**84**	**117**
Fruquintinib, (VEGFR 1/2/3) ELUNATE	2	3	5	6	11	17
Surufatinib (VEGFR 1/2/3, FGFR1 & CSF-1R)			-	24	73	97
Savolitinib (c-MET)			-	0	0	3
Services	**26**	**16**	**8**	**31**	**10**	**17**
Services - Commercialization – ELUNATE	-	-	(2)	6	10	17
Services - Collaboration R&D - third parties	18	16	10	25	-	-
Services - R&D services - related parties	8	0	0	-	-	-
Other collaboration revenue	**12**	**3**	**5**	**19**	**32**	**77**
Royalties - third parties	0	3	5	19	32	77
Licensing - third parties	12	-	-	-	-	-
Other Ventures	**31**	**23**	**21**	**22**	**23**	**24**
Goods - Third parties	27	22	21	22	23	24
Services - Commercialization - third parties	3	1	-	-	-	-
Total	**70**	**45**	**39**	**102**	**150**	**236**
GPM (%)						
Oncology/Immunology	***96%***	***82%***	***60%***	***63%***	***61%***	***62%***
Goods	***53%***	***40%***	***46%***	***57%***	***66%***	***61%***
Fruquintinib, (VEGFR 1/2/3) ELUNATE	*53%*	*40%*	*46%*	*30%*	*32%*	*33%*
Surufatinib (VEGFR 1/2/3, FGFR1 & CSF-1R)	-	-	-	*80%*	*81%*	*82%*
Savolitinib (c-MET)	-	-	-	*10%*	*12%*	*13%*
Services	***100%***	***100%***	***57%***	***57%***	***22%***	***24%***
Services - Commercialization – ELUNATE	-	-	*(61)%*	*20%*	*22%*	*24%*
Services - Collaboration R&D - third parties	*100%*	*100%*	*100%*	*100%*	-	-
Services - R&D services - related parties	*100%*	*100%*	*100%*	-	-	-
Other collaboration revenue	***100%***	***100%***	***100%***	***100%***	***100%***	***100%***
Royalties - third parties	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Licensing - third parities	*100%*	-	-	-	-	-
Other Ventures	***18%***	***13%***	***11%***	***11%***	***11%***	***11%***
Goods - Third parties	*17%*	*13%*	*11%*	*11%*	*11%*	*11%*
Services - Commercialization - third parties	*26%*	*25%*	-	-	-	-
Total	***33%***	***22%***	***17%***	***31%***	***35%***	***42%***

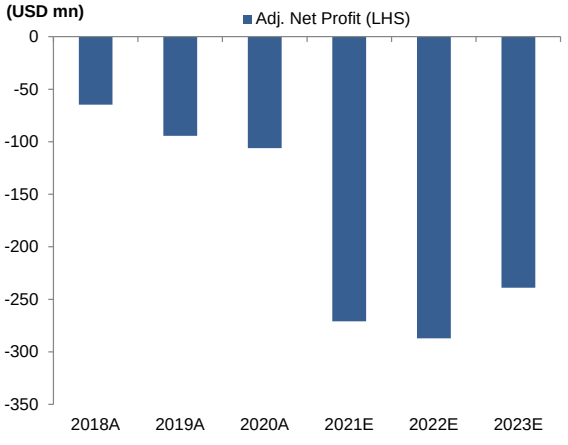
Sources: Company, CMS (HK) estimates

Figure 73: Gross margin trend



Sources: Company, CMS (HK) estimates

Figure 74: Adj. net profit trend



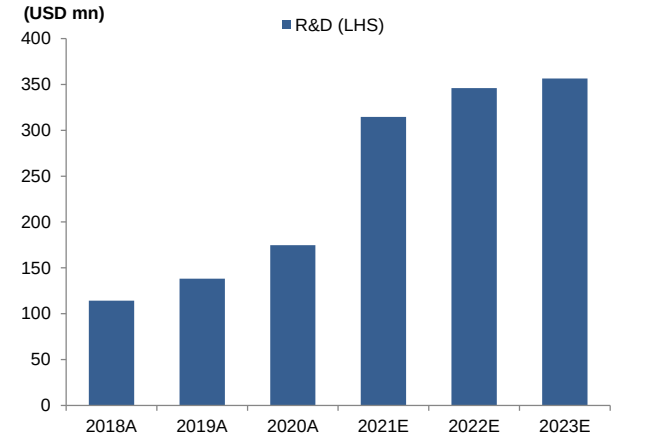
Sources: Company, CMS (HK) estimates

Research and Development expenses, and Capital Expenditure

HCM recorded research and development expenses at USD114mn/138mn/175mn over 21018-20. R&D expenses are largely attributable to HCM Oncology/Immunology operations. These costs primarily comprise the cost of research and development for its drug candidates, including clinical trial related costs such as payments to third-party CROs, personnel compensation and related costs, and other research and development expenses. With label expansion efforts and a comprehensive early-stage R&D pipeline, we predict that the R&D expenses should reach USD315mn/346mn/356mn in 2021E-23E. As such, Company should maintain a net loss in the near future.

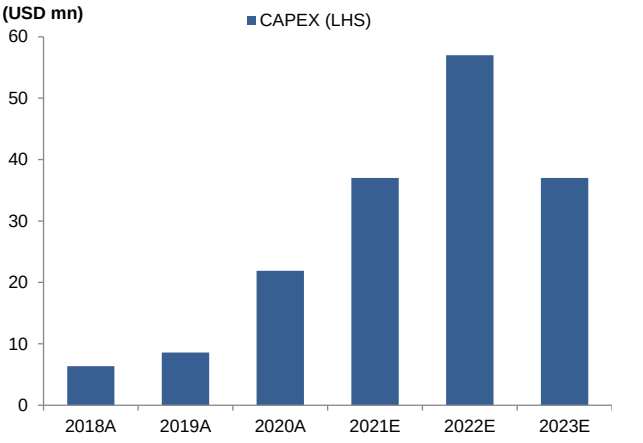
HCM had capital expenditures of ~USD6mn/9mn/20mn over 2018-2020. HCM capital expenditures during these periods were primarily used for the maintenance CAPEX, the PP&E to expand the Hutchison MediPharma research facilities and the manufacturing facility in Suzhou, China, and the acquisition of leasehold land in 2020 for a new large-scale manufacturing facility for innovative drugs in Shanghai, China. Co. expects a total CAPEX of USD130mn for Shanghai factory over 5 years in addition to a USD15-20mn of maintenance CAPEX. We thus predict that the annual CAPEX should reach an average of ~USD40-50mn over 5 years.

Figure 75: R&D expense and trend (USD mn)



Sources: Company, CMS (HK) estimates

Figure 76: CAPEX and forecast (USD mn)



Sources: Company, CMS (HK) estimates

Appendix: Management Summary

Chairman, Mr. Chi Keung Simon To, aged 69, joined the Company in 2000. He was appointed as an executive director and the chairman of the Board of the company since 2006. He is the managing director of Hutchison Whampoa (China) Limited and has been with Hutchison Whampoa (China) Limited for more than four decades. He is the original founder of the China healthcare business of Hutchison Whampoa Limited (currently a subsidiary of CK Hutchison).

Mr. To received an MBA degree from Stanford University in the US in 1975.

Chief Executive Officer, Mr. Christian Hogg, aged 56, joined the Company in 2000 as the 1st employee. He was appointed as an executive director and the CEO of the company since 2006 and has since led the planning, execution and management of Co.'s oncology/IO businesses and other ventures. Mr. Hogg has extensive industry experience. Prior to joining the Company, Mr. Hogg spent 10 years at P&G prior joining the company.

Mr. Hogg received a MBA degree from the University of Tennessee in the US in 1989.

Chief Financial Officer, Mr. Chig Fung Jonny Cheng, aged 54 joined company as the CFO since 2008 and was appointed as an executive director since 2011. Mr. Cheng has extensive industry experience in the pharmaceutical industry. Prior to joining the Company, Mr. Cheng worked as the VP of finance at BMS China as well as directors at Shanghai Squibb and BMS China investment in Shanghai between 2006 and 2008. Mr. Cheng started his career as an auditor at Price Waterhouse (nowadays PwC) in Australia in 1989. He was also in charge of a number of finance and control functions at various companies.

Mr. Cheng completed a Bachelor of Economics degree at the University of Adelaide in Australia in 1988. He is a member of the Chartered Accountants Australia and New Zealand since 1992.

Chief Scientific Officer, Dr. Wei-guo Su, aged 64, joined the Company in 2005. He was appointed the CSO of the company since 2012 and an executive directors since 2017. Dr. Su has headed all drug discovery and research since he joined the company. Dr. Su has extensive industry experience. Prior to joining the Company, Dr. Su worked at the R&D department of Pfizer in the US.

Dr. Su completed a Ph.D. degree and post-doctoral fellowship in chemistry at Harvard University in the US in 1988.

Financial Summary

Balance Sheet

USD mn	2019	2020	2021E	2022E	2023E
Non-current assets	**154**	**232**	**280**	**154**	**232**
PP&E	54	95	105	54	95
Intangible assets	8	8	8	8	8
Prepaid lease payments	-	-	-	-	-
Deferred tax assets	2	2	2	2	2
Others	20	20	20	20	20
Current assets	**1,258**	**887**	**596**	**1,258**	**887**
Inventories	24	29	35	24	29
Loan and account receivables	59	79	96	59	79
Prepayments and other receivables	27	27	27	27	27
Assets held-for-sale	1	1	1	1	1
Short-term investments	200	200	200	200	200
Bank balances and cash	947	552	238	947	552
Total assets	**1,412**	**1,119**	**876**	**1,412**	**1,119**
Current liabilities	**165**	**172**	**181**	**165**	**172**
Trade and bills payables	38	45	54	38	45
Due to a related party	121	121	121	121	121
ST bank debt	-	-	-	-	-
Others	3	3	3	3	3
Non-current liabilities	**147**	**147**	**147**	**147**	**147**
Long-term payables	-	-	-	-	-
Contract liabilities	5	5	5	5	5
LT bank loans	127	127	127	127	127
Others	14	14	14	14	14
Shareholders' funds	**1,057**	**749**	**487**	**1,057**	**749**
Minorities	**43**	**52**	**60**	**43**	**52**
Total liability and equity	**1,412**	**1,119**	**876**	**1,412**	**1,119**

Cashflow Statement

USD mn	2019	2020	2021E	2022E	2023E
Operating cash flow	**(81)**	**(62)**	**(346)**	**(357)**	**(289)**
Pretax profit	(104)	(116)	(304)	(300)	(253)
Operating profit before WC chg	(97)	(91)	(336)	(336)	(271)
Net working capital change	16	29	(9)	(17)	(14)
Income tax paid	-	-	-	-	-
Interest paid	-	-	(1)	(4)	(4)
Investing cash flow	**119**	**(125)**	**323**	**(38)**	**(26)**
Purchase of PPE	(9)	(8)	(37)	(57)	(37)
Purchase/disposal of subsidiaries	9	-	-	-	-
Purchase/disposal of JV&Asso.	-	-	305	-	-
Interest received	-	-	5	19	11
Others	119	(104)	50	-	-
Financing cash flow	**(1)**	**296**	**735**	**-**	**-**
Proceeds from IPO net of fees	0	311	635	-	-
Issurance of equity shares	-	-	-	-	-
Proceeds/repayment of bank borrowings	(0)	-	100	-	-
Others	-	-	-	-	-
Beginning cash	**86**	**121**	**236**	**947**	**552**
Forex	*(2)*	*6*	-	-	-
End cash	**121**	**236**	**947**	**552**	**238**

Profit & Loss

USD mn	2019	2020	2021E	2022E	2023E
Consolidated revenue	**205**	**228**	**334**	**425**	**567**
Cost of goods sold	(160)	(189)	(232)	(275)	(332)
Gross profit	**45**	**39**	**102**	**150**	**236**
(–) Total SG&A expense	(53)	(61)	(111)	(151)	(173)
Administrative expenses	(39)	(50)	(61)	(73)	(81)
Selling and distribution costs	(14)	(11)	(51)	(78)	(92)
(–) R&D expense	(138)	(175)	(315)	(346)	(356)
(+/–) Other income/expense	-	-	-	-	-
(+/–) Profit from JV&Asso.	41	79	35	37	39
Adj. EBITDA	**(89)**	**(92)**	**(255)**	**(273)**	**(205)**
Stock-Based Compensation	(12)	(20)	(27)	(21)	(23)
Total Depreciation and amortisation	(5)	(6)	(7)	(16)	(28)
Adj. EBIT	**(94)**	**(98)**	**(262)**	**(289)**	**(232)**
(+/–) Finance expense - net	4	2	4	15	7
(+/–) Others, net	1	4	(14)	-	-
Profit before tax	**(100)**	**(111)**	**(299)**	**(295)**	**(248)**
(–) Tax	(3)	(5)	(5)	(5)	(5)
Net Profit	(104)	(116)	(304)	(300)	(253)
(+/–) Minority interest	(2)	(10)	(8)	(9)	(9)
Attributable net profit	**(106)**	**(126)**	**(312)**	**(308)**	**(262)**
Adjusted net profit	**(94)**	**(106)**	**(271)**	**(287)**	**(239)**
EPS Fully diluted (USD)	**(0.14)**	**(0.15)**	**(0.35)**	**(0.34)**	**(0.28)**

Financial Ratios

	2019	2020	2021E	2022E	2023E
Growth (%)					
Consolidated revenue	(4%)	11%	47%	27%	34%
Gross profit	(36%)	(12%)	160%	47%	57%
Adjusted net profit	n.a.	n.a.	n.a.	n.a.	n.a.
Profitability (%)					
Gross margin (%)	22%	17%	31%	35%	42%
Adj. net profit margin (%)	n.a.	n.a.	n.a.	n.a.	n.a.
ROE	n.a.	n.a.	n.a.	n.a.	n.a.
ROA	n.a.	n.a.	n.a.	n.a.	n.a.
Efficiency					
Inventory days	32	34	35	35	35
Accounts receivable days	88	81	77	74	77
Accounts payable days	56	53	55	55	55
Cash cycle days	64	62	56	54	57
Liquidity					
FCF (RMB mn)	(89)	(84)	(383)	(414)	(326)
Net gearing (%)	(29)	(40)	(74)	(53)	(20)

Sources: Company data, CMS (HK) estimates

Investment Ratings

Industry Rating	Definition
OVERWEIGHT	Expect sector to outperform the market over the next 12 months
NEUTRAL	Expect sector to perform in-line with the market over the next 12 months
UNDERWEIGHT	Expect sector to underperform the market over the next 12 months

Company Rating	Definition
BUY	Expect stock to generate 10%+ return over the next 12 months
NEUTRAL	Expect stock to generate +10% to -10% over the next 12 months
SELL	Expect stock to generate loss of 10%+ over the next 12 months

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China Merchants Securities (HK) Co., Ltd.
Address: 48/F, One Exchange Square, Central, Hong Kong
Tel: +852 3189 6888 Fax: +852 3101 0828