HUTCHMED (13 HK)

A home-grown, global-facing Biopharma

- **Global biopharma with strong in-house R&D platform.** Founded in 2000, HUTCHMED (HCM) is a global biopharma with strong in-house R&D platform in developing targeted therapies in oncology and immunology. HCM has assembled a highly differentiated pipeline of 13+ assets under clinical development/ IND-enabling stage, three of which have been launched in China, namely, savolitinib, fruquintinib and surufatinib. We view value creation of HCM is driven by label expansion opportunities of the three launched products, along with advancement of next-wave innovative assets, namely HMPL-689 (PI3Kδ inhibitor), HMPL-523 (SYK inhibitor), HMPL-453 (pan-FGFR inhibitor), HMPL-306 (IDH1/2 inhibitor), and HMPL-295 (ERK inhibitor).
- **A highly differentiated, synergistically designed pipeline.** HCM has built a highly differentiated pipeline with four competitive features: i) adopting a multi-prolonged approach targeting therapeutic pathways of angiogenesis, epigenetics and immuno-oncology (I/O), allowing for synergies within its internal pipeline and potential future assets; ii) an expanding pipeline of five fast-progressing early-to-mid stage assets with first-in-class/ best-in-class potential, namely, HMPL-689 (PI3Kδ inhibitor), HMPL-523 (SYK inhibitor), HMPL-453 (pan-FGFR inhibitor), HMPL-306 (IDH1/2 inhibitor), and HMPL-295 (ERK inhibitor); iii) validated targets of aforementioned novel assets, and iv) global clinical advancement to maximize its global market potential.
- **Well-established commercial infrastructure.** HCM has assembled an oncology commercial team of 540 personnel covering over 2,500 oncology hospitals in China as of mid-2021, with a plan to expand to 600/900 personnel by 2021E/2023E.The team is dedicated to support market launches of Elunate, Sulanda, along with other innovative drugs down the road in China. Moreover, with hematology assets advancing further along the pipeline, build-out of China hematology commercial team is under planning.
- **Initiate at BUY with TP of HK$77.74.** We forecast total revenue to reach US$340mn/ US$423mn/ US$561mn in FY2021E/ 22E/ 23E, representing a YoY growth of 49%/ 25%/ 33%. We expect increasing revenue contribution from the innovative immunology/oncology platform, mainly driven by sales ramp-up of savolitinib, fruquintinib and surufatinib in the near-term. We derive our target price of HK$77.74 based on a 15-year DCF valuation (WACC: 9.07%, terminal growth rate: 4%). We expect HCM to generate positive free cash flows starting 2025E.
- **Key risks:** Delay in pipeline advancement; disappointing clinical data readouts; failure of commercial execution.

Earnings Summary

(YE 31 Dec)	FY19A	FY20A	FY21E	FY22E	FY23E
Revenue (US$ mn)	205	228	340	423	561
YoY growth (%)	(4)	11	49	25	33
Net loss (US$ mn)	(106)	(126)	(220)	(277)	(225)
EPS (US$)	(0.16)	(0.18)	(0.25)	(0.32)	(0.26)
Consensus EPS (US$)	N/A	N/A	(0.73)	(0.65)	(0.28)
R&D expenses (US$ mn)	(138)	(175)	(300)	(330)	(350)
Capex (US$ mn)	(9)	(8)	(35)	(50)	(10)

Source: Company data, Bloomberg, CMBIS estimates

BUY (Initiation)

Target Price	HK$77.74
Up/Downside	+30.22%
Current Price	HK$59.70

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Mkt. Cap. (HK$ mn)	51.60
Avg. 3mths t/o (HK$ mn)	N/A
52W High/Low (HK$)	85.8/51.2
Total Issued Shares (mn)	864

Source: Bloomberg

Shareholding Structure

CK Hutchison Holdings	39.19%
The Capital Group	9.14%
JP Morgan	6.91%
Free float	44.75%

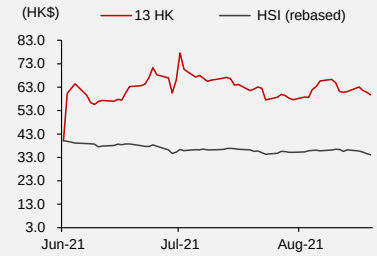
Source: HKEx, Bloomberg

Share performance

	Absolute	Relative
1-mth	-5.2%	-0.1%
3-mth	N/A	N/A
6-mth	N/A	N/A

Source: Bloomberg

12-mth price performance



Source: Bloomberg

Auditor: PricewaterhouseCoopers
Web-site: https://www.hutch-med.com

Contents

Investment Thesis

Founded in 2000, HUTCHMED (HCM) is a global biopharma with comprehensive in-house R&D platform focusing on the discovery, development and commercialization of targeted therapies in oncology and immunology. The Company primarily operates two platforms, i) drug innovation platform and ii) drug selling and distribution platform. HCM was listed on AIM since 2006 and on NASDAQ since 2016. In Jun 2021, HCM was listed on HKEX.

Highly differentiated, synergisticallsy designed asset portfolio

HCM has assembled a highly differentiated pipeline of 13+ assets under clinical development/ IND-enabling stage, including three launched products, namely, savolitinib (Orpathys), fruquintinib (Elunate) and surufatinib (Sulanda).

Approved in Jun 2021, savolitinib (Orpathys) is China's first and solely approved, highly selective MET inhibitor for NSCLC with MET exon14 skipping alternation. The key to unleashing its market potential, in our view, lies in global label expansion opportunities in EGFR inhibitor refractory NSCLC. Approximately 30% Targrisso-treated 2/3L EGFRm+ NSCLC patients further develop MET aberrations, while the current therapeutic option for this group of patients represents a black hole. We model risk-adjusted global sales of US$1.08bn for savolitinib with US$322mn in revenue attributable to HCM in 2030E, risk-adjusted global peak sales of US$1.18bn with US$348mn in revenue attributable to HCM in 2033E.

Surufatinib (Sulanda) is the first VEGFR/FGFR/CSF-1 small molecule inhibitor for treating all types of grade 1/2 neuroendocrine tumors (NETs), with the non-pancreatic NET (npNET) and pancreatic NET (pNET) indication approved by the China NMPA in Dec 2020 and Jun 2021, respectively. Globally, NDA submission to the US FDA and MAA filing to the EU EMA for all types of grade 1/2 NETs were both accepted in Jul 2021. We view surufatinib's broad patient eligibility as a key differentiator since none of targeted therapies have been approved for all types of NETs worldwide. Surufatinib is also being explored in combination with various PD-1 mAbs including Junshi's toripalimab, Innovent's sintilimab and BeiGene's tislelizumab, across multiple solid tumor indications in China and globally, with a near-term plan to initiate a Phase III trial for neuroendocrine carcinoma (NEC) in China in 2H21E. We forecast surufatinib to generate risk-adjusted global sales of US$978mn in 2030E, and risk-adjusted global peak sales of US$1.00bn in 2032E.

Fruquintinib (Elunate) is a highly selective VEGFR 1/2/3-targeted small molecule inhibitor approved in China in Sep 2018 as 3L treatment fors advanced colorectal cancer (CRC). It has been included in NRDL since Jan 2020. Fruquinitib recorded in-market sales of US$33.7mn/US$40.1mn in 2020/1H21, up 91.5%/186% YoY respectively. Featured by its optimized kinase selectivity and clean safety profile, fruquintinib provides a strong basis for combination option with PD-1 mAb as well as other internal pipeline assets. The Company is pursuing label expansion opportunities for fruquintinib in 3L CRC in a global Phase III trial, and multiple solid tumor indications in combination with various PD-1 mAbs (including Beigene's tislelizumab, Genor's geptanolimab and Innovent's sintilimab) in China and globally. We forecast fruquintinib to record risk-adjusted, attributable global sales of US$1.07bn in 2030E, and risk-adjusted attributable global peak sales of US$1.09bn in 2031E.

HCM's pipeline is strategically designed with competitive features: i) adopting a multi-prolonged approach targeting therapeutic pathways of angiogenesis, epigenetics and immuno-oncology (I/O), allowing for synergies within its internal pipeline and potential future assets; ii) an expanding pipeline of five fast-progressing early-to-mid stage assets with first-

in-class/sbest-in-class potential, namely, HMPL-689 (PI3Kδ inhibitor), HMPL-523 (SYK inhibitor), HMPL-453 (pan-FGFR inhibitor), HMPL-306 (IDH1/2 inhibitor), and HMPL-295 (ERK inhibitor); iii) validated targets of aforementioned novel assets, and iv) global clinical development to maximize its global market potential.

Comprehensive, globally endorsed in-house R&D engine

Featured by its comprehensive in-house R&D platform covering chemistry, biology, pharmacology, toxicology, chemistry and manufacturing (CMC) controls, HCM adopts a long-standing R&D strategy to build its oncology and immunology franchise. As a home-grown, globally-facing drug discovery platform, HCM is a pioneer among China biopharma peers that out-licensed two internally developed assets, namely, savolitinib (global rights to AstraZeneca) and fruquintinib (China rights to Eli Lily). HCM has built an R&D team comprising of approximately 720 scientists and employees located in Shanghai and Suzhou in China, and New Jersey in the US.

Well-established commercial infrastructure

HCM has assembled an oncology commercial team of 540 personnel, covering over 2,500 oncology hospitals and 29,000 oncology physicians in China as of mid-2021. The team is dedicated to support China market launches of Elunate, Sulanda, along with other innovative drugs down the road. The Company aims to expand its China commercial team to 600/900 personnel by 2021E/2023E, respectively, as per management. Moreover, with hematology assets advancing further along the pipeline, a near-term build-out of China hematology commercial team is under planning.

Expanding in-house manufsacturing capabilities

HCM has established a GMP-certified production facility in Suzhou, supporting commercial sales of Elunate and Sulanda, and other drug candidates for clinical trials. To meet the manufacturing demand for upcoming product launches, HCM has commenced construction of a 55,000m² large-scale manufacturing plant in Shanghai. The first Phase will be primarily for small molecule production, while the second phase is planned for large molecule drug production.

Initiate at BUY with TP of HK$77.74

We forecast total revenue to reach US$340mn/ US$423mn/ US$561mn in FY2021E/ 22E/ 23E, representing a YoY growth of 49%/ 25%/ 33%. We expect increasing revenue contribution from the innovative immunology/oncology platform, mainly driven by sales ramp-up of savolitinib, fruquintinib and surufatinib in the near-term. We derive our target price of HK$77.74 based on a 15-year DCF valuation (WACC: 9.07%, terminal growth rate: 4.0%).

Investment risks

1) Clinical development risks: Positive early study results may not be predictive of later-stage trial's success. Any failure in HCM's pipeline's ongoing trials may potentially result in failure in product approval.

2) Regulatory approval risks: The Company's ability to generate revenue will depend primarily on the successful regulatory approvals of its pipeline assets.

3) Competition risk: The Company may be exposed to fierce competition as competitors may develop and commercialize drugs ahead of the curve leading to market saturation.

Biopharma company with global operation

Founded in 2000 by Hutchison Whampoa (which became a wholly-owned subsidiary of CK Hutchison in 2015), HUTCHMED (HCM) is a global biopharma with in-house drug discovery engine focusing on the discovery, development and commercialization of targeted therapies in oncology and immunology. The Company was listed on AIM since 2006 and on NASDAQ since 2016. In Jun 2021, HCM was listed on HKEX.

In Apr 2020, the Company consolidated two corporate identities, namely, Hutchison China MediTech (or Chi-Med, which has been used as the group identity) and Hutchison MediPharma (which has been the identity of novel drug R&D operations), with brand name changed from Chi-Med to HCM.

HCM has established a fully integrated drug discovery platform since the launch of its oncology/immunology operations in 2002. As these innovations progressed, HCM has added extensive clinical and regulatory, manufacturing and commercial operations resulting in a fully-integrated biopharmaceutical company of over 1,300 personnel as of mid-2021. Over the past 15 years, HCM's in-house discovery engine has created a broad pipeline of ten clinical stage drug candidates with a further seven oncology and immunology drug candidates in preclinical testing. HCM's highly differentiated drug candidates have achieved collaborations with leading global pharmaceutical companies such as AstraZeneca and Eli Lilly.

Beyond oncology/immunology operations, the Company also engages with the selling and distribution of precision drugs and consumer health products through joint venture operations including Shanghai Hutchison Pharmaceuticals (SHPL, 上海和黄药业), Hutchison Sinopharm (国控和黄), Hutchison Baiyunshan (HBYS, 白云山和黄), etc. The Company's large-scale drug marketing and distribution platforms cover 320 cities and counties in China with 4,700 aggregate manufacturing and commercial personnel as of mid-2021. In Mar 2021, HCM announced to sell its entire indirect interest in HBYS to GL Capital at approximately US$159mn in cash.

Figure 1: Key development milestones

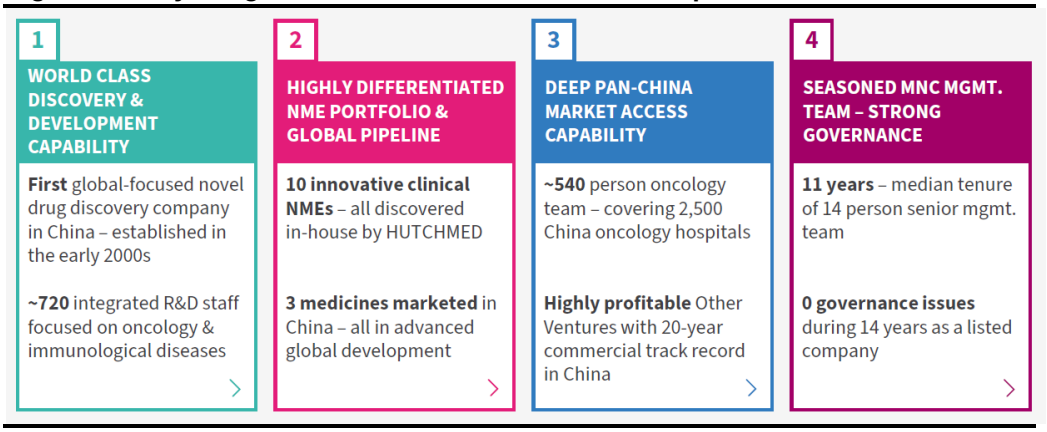
Year	Event
2001	• Established Shanghai Hutchison Pharmaceuticals, a JV with Shanghai Pharmaceuticals to manufacture market and distribute prescription drug products • Established Hutchison Healthcare, a JV which subsequently become a wholly owned subsidiary in 2009, to manufacture and sell health supplements
2002	• Launched Oncology/Immunology operations with the establishment of subsidiary HMPL
2005	• Commenced small molecule drug research • Established Hutchison Baiyuanshan, a JV with Guangzhou Baiyunshan, to manufacture, market and distribute OTC pharmaceutical products
2006	• Traded on AIM
2006-2008	• Entered into research collaborations with Merck, Eli Lilly, and Ortho-McNeil Janssen, focusing on novel small molecule oncology drugs
2011	• Entered into global research collaborations with AstraZeneca to co-develop and commercialize savolitinib
2013	• Entered into collaboration with Eli Lily in China to co-develop and commercialize fruquintinib
2014	• Established Hutchison Sinopharm, a JV with Sinopharm to provide logistics services to distribute and market prescription drugs
2016	• Listed on NASDAQ
2018	• Elunate (fruquintinib) was approved by NMPA for the treatment of mCRC and launched partnership with Eli Lily in China • Entered into co-development collaborations for fruquintinib and surufatinib in combination with various PD-1 mAb, including Junshi's toripalimab and Innovent's sintilimab • Expanded the US and international clinical and regulatory operations- established US based in New Jersey
2019	• Elunate (fruquintinib) included in NRDL in Nov 2019, effective from Jan 2020 • Established China oncology commercial organization

2020	• Entered into clinical collaboration agreement with BeiGene for fruquintinib and surufatinib in combination with tislelizumab in the US, Europe, China and Australia • Entered into an amendment collaboration agreement on fruquintinib with Eli sLily to cover the promotion and marketing of Elunate (fruquinitib) in China by NMPL from Oct 2020 • Sulanda (surufatinib) was approved by NMPA for advanced non-pancreatic NETs
2021	• Launched Sulanda (surufatinib) for advanced non-pancreatic NETs in China • Sold all interests in Hutchison Baiyunshan • Changed group identify from Chi-Med to HUTCHMED • Announced its inclusion in several Hang Seng indexes, including Hang Seng Composite Index effective from 6 Sep 2021, Hang Seng Healthcare Index and Hang Seng Hong Kong-Listed Biotech Index, Seng Stock Connect China 500 Index thus eligible for Northbound or Southbound trading under the Stock Connect schemes

Source: Company data, CMBIS

HCM has a comprehensive drug discovery and development operation covering chemistry, biology, pharmacology, toxicology, chemistry and manufacturing controls for clinical and commercial supply, clinical and regulatory and other functions. It is led by a team of approximately 720 scientists and staff as mid-2021. HCM is conducting and planning over 40 different clinical studies in oncology patients globally, including plans for ten Phase III registration and Phase II registration-intent studies underway by the end of 2021.

Figure 2: Fully integrated R&D and commercialization platform



Source: Company data, CMBIS

Highly differentiated, synergistically designed asset portfolio

HCM has assembled a highly differentiated pipeline of 13+ assets at clinical development/IND-enabling stage, including three marketed products, namely, savolitinib (Orpathys), fruquintinib (Elunate) and surufatinib (Sulanda).

Approved by NMPA in Jun 2021, savolitinib (brand name: Orpathys) is the first and solely approved, highly selective MET inhibitor for NSCLC with MET exon14 skipping alternation (occurring in 3-4% of NSCLC patients) in China. The key to unleashing its market potential, in our view, lies in the next wave of global label expansion opportunities in EGFR inhibitor refractory NSCLC, including i) 2L EGFRm+, TKI refractory MET+ NSCLC in China, ii) naive EGFRm+, MET+ NSCLC in China, and iii) 2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC in the US/EU/Japan, in combination with Tagrisso (3rd-gen EGFR inhibitor). Approximately 30% of Targrisso-treated 2/3L EGFRm+ NSCLC patients further develop MET aberrations, and the therapeutic option for these patients represents a black hole. Savolitinib is poised to unlock its global market potential in Tagrisso refractory NSCLC, benefiting from the uptrend in Tagrisso sales momentum with US$4.33bn global sales in 2020 and estimated peak sales of US$8bn in 2025, according to AstraZeneca. Upon out-

licensing worldwide development and commercialization rights to AstraZeneca, HCM is entitled to receive 30% fixed royalties on China sales, along with development fees, commercial milestones and manufacturing fees paid by AstraZeneca, and up to 14%-18% tiered royalties on ex-China sales.

Surufatinib (brand name: Sulanda) is China's first VEGFR/FGFR/CSF-1 small molecule inhibitor for treating all types of grade 1/2 neuroendocrine tumors (NETs), with its non-pancreatic NET (npNET) and pancreatic NET (pNET) indications approved by the NMPA in Dec 2020 and Jun 2021, respectively. Globally, NDA submission to the US FDA and MAA filing to the EU EMA for all types of grade 1/2 NETs were both accepted in Jul 2021. Although NET is a small indication with 71,300/19,700 new cases in China/ the US in 2020, we think surufatinib's broad patient eligibility is a key differentiator given none of targeted therapies have been approved for all types of NETs globally. Thanks to its dual-blocking MoA which can potentially amplify PD-1 mAb-induced anti-tumor activity, surufatinib is being explored in various Phase I/II trials in combination with Junshi's JS001 (PD-1) and BeiGene's tislelizumab (PD-1) across multiple solid tumor indications in China and globally. Within the basket trials in combination with PD-1 mAb, neuroendocrine carcinoma (NEC) is planned to be advanced first and is expected to commence a Phase III trial in China in 2H21E. HCM owns global rights of surufatinib, which is currently being marketed by HCM's in-house oncology commercial team in China.

Fruquintinib (brand name: Elunate) is a highly selective VEGFR 1/2/3-targeted small molecule inhibitor approved in China in Sep 2018 as 3L treatment for advanced colorectal cancer (CRC). It has been included in the NRDL since Jan 2020. Fruquintinib recorded in-market sales of US$33.7mn/US$40.1mn in 2020/1H21, up 91.5%/186% YoY respectively. Featured by its superior kinase selectivity and clean safety profile, Elunate provides a strong basis for combination options with PD-1 mAb or other internal pipeline assets such as Tazeverik (tazemetostat/EZH2 inhibitor). The Company is pursuing label expansion opportunities in 3L CRC in a global Phase III trial and multiple solid tumor indications in combination with various PD-1 mAbs (including BeiGene's tislelizumab, Genor's geptanolimab and Innovent's sintilimab) in Phase I/II trials in China and globally. With China rights out-licensed to Eli Lily in Oct 2013, Elunate had been commercialized by Eli Lily until Oct 2020 when HCM assumed its commercial responsibility. HCM retains ex-China rights in Elunate, while being entitled to receive 70-80% of Elunate China sales in form of royalties, manufacturing cost and additional service payments of associated commercialization payment from Eli Lily.

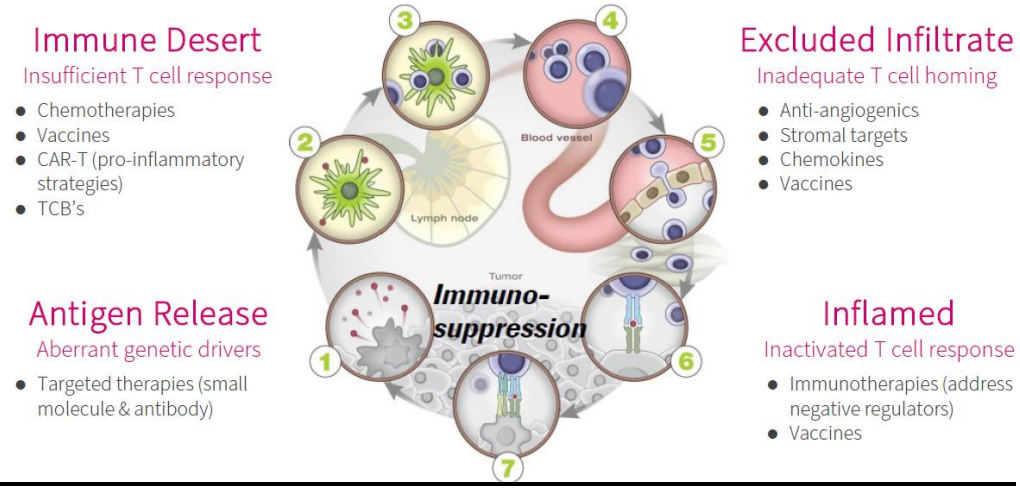
Figure 3: HCM's differentiated asset portfolio

PRODUCT	MOA	DISCOVERY[1]	INDICATIONS	PARTNER	RIGHTS	CHINA[2]	GLOBAL[2]
Surufatinib (SULANDA®)	VEGFR 1/2/3, FGFR1 & CSF-1R	In-house (est. LOE ~2035)	Neuroendocrine tumors (NET), biliary tract, thyroid, solid tumors (multiple I/O combos)	None	HCM holds all WW rights	**Marketed** (non-pNET) **Marketed** (pNET)	**U.S. NDA accepted** **E.U. MAA accepted**
Fruquintinib (ELUNATE®)	VEGFR 1/2/3	In-house (est. LOE ~2033)	Colorectal, gastric, NSCLC, solid tumors (multiple I/O & TKI combos)	Lilly	HCM has WW rights ex-China; 70%-80% of sales in China [4]	**Marketed** (Colorectal); **Ph.III** (Gastric)	**Ph.III U.S., E.U., Japan** (Colorectal)
Savolitinib (ORPATHYS®)	MET	In-house (est. LOE ~2035)	NSCLC, kidney, gastric [3], colorectal[3] (multiple I/O & TKI combos)	AZ	AZ has WW rights; China (30% royalty); ex-China (9-18% tiered royalty)	**Marketed** (NSCLC mono) **Ph.III** (GC, NSCLC combo*)	**Ph.II/III global** (multiple NSCLC) **Ph.III global** (PRCC*)
HMPL-689	PI3Kδ	In-house (est. LOE ~2040)	B-cell malignancies – indolent NHL	None	HCM holds all WW rights	**Ph.II reg-intent** (FL & MZL)	**Ph.I** U.S., E.U., Aus (NHL)
HMPL-523	Syk	In-house (est. LOE ~2037)	ITP, B-cell malignancies – indolent non-Hodgkin's lymphoma (NHL)	None	HCM holds all WW rights	**Ph.Ib/II** (Treated >200 NHL pts.)	**Ph.I** U.S., E.U., Aus (NHL)
HMPL-453	FGFR 1/2/3	In-house (est. LOE ~2039)	Cholangiocarcinoma	None	HCM holds all WW rights	**Ph.II** (IHCC)	-
Epitinib	EGFRm+	In-house (est. LOE ~2032)	Glioblastoma	None	HCM holds all WW rights	**Ph.II** (Glioblastoma)	-
HMPL-306	IDH 1/2	In-house (est. LOE ~2043)	Hematological malignancies, solid tumors	None	HCM holds all WW rights	**Ph.I** (Hem. malignancies)	**Ph.I** (solid tumor & hem. malignances)
HMPL-295	ERK (MAPK pathway)	In-house	Solid tumors	None	HCM holds all WW rights	**Ph.I** (Solid tumors)	-
HMPL-760	3G BTK	In-house	Hematological malignancies	None	HCM holds all WW rights	IND submitted June 2021	IND submitted June 2021
HMPL-653	CSF-1R	In-house	Solid tumors	None	HCM holds all WW rights	Target IND 2021 (U.S./China)	
HMPL-A83	CD47	In-house	mAb – solid tumors, hematological malignancies	None	HCM holds all WW rights	Target IND 2021 (U.S./China)	

Source: Company data, CMBIS

HCM's pipeline is strategically designed with competitive features: i) adopting a multi-prolonged approach targeting therapeutic pathways of angiogenesis, epigenetics and immuno-oncology (I/O), allowing for synergies within its internal pipeline and potential future assets; ii) an expanding pipeline of five fast-progressing early-to-mid stage assets with first-in-class/-best-in-class potential, namely, HMPL-689 (PI3Kδ inhibitor), HMPL-523 (SYK inhibitor), HMPL-453 (pan-FGFR inhibitor), HMPL-306 (IDH1/2 inhibitor), and HMPL-295 (ERK inhibitor); iii) validated targets of aforementioned novel assets de-risking clinical advancement, and iv) global trial expansion to maximize its global market potential.

Figure 4: HCM's long-standing R&D strategy



Source: Company data, CMBIS

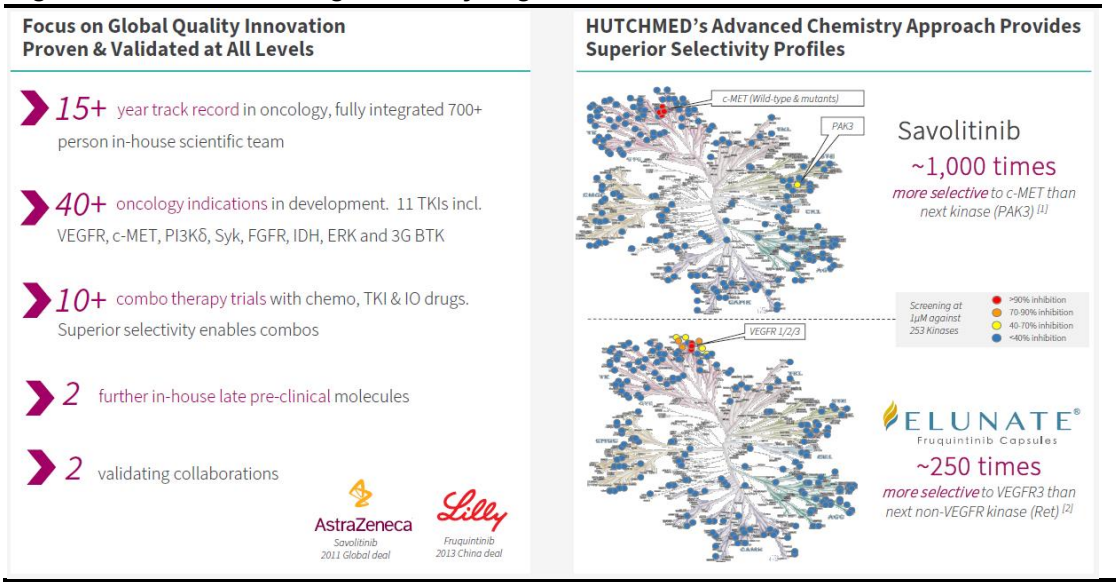
Comprehensive, globally endorsed in-house R&D engine

Featured by its comprehensive in-house R&D platform covering chemistry, biology, pharmacology, toxicology, chemistry and manufacturing (CMC) controls, HCM adopts a long-standing R&D strategy of assembling high quality assets against novel targets in oncology and immunology. As a home-grown, globally-facing drug discovery platform, HCM is one of the first China biopharma companies that landed two collaborations, with

two internally developed assets, namely, savolitinib and fruquintinib, out-licensed to MNCs (AstraZeneca and Eli Lily), which showcased global endorsement of its R&D capabilities.

HCM has built an R&D team comprising of approximately 720 scientists and employees based in Shanghai and Suzhou in China, and New Jersey in the US, of which over 350 had advanced degrees (including 30+ had M.D.s and 80+ had doctorate degrees) as of 1H21.

Figure 5: World-class drug discovery engine

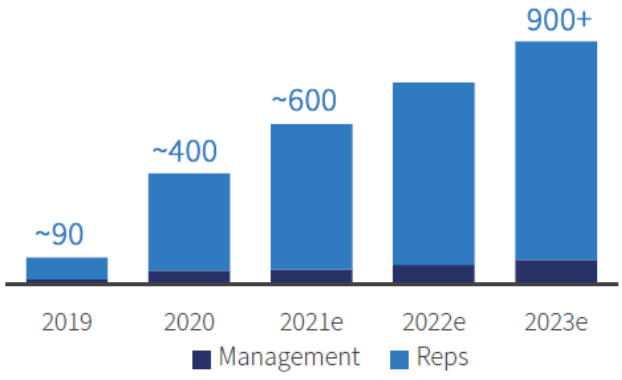


Source: Company data, CMBIS

Well-established commercial infrastructure

HCM has assembled an oncology commercial team of 540 personnel, covering over 2,500 oncology hospitals/clinics and over 29,000 oncology physicians in China as of 1H21. The team is dedicated to support China market launches of Elunate, Sulanda, along with other innovative drugs down the road. The Company aims to expand its China commercial team to 600/900 personnel by the end of 2021E/2023E, respectively.

Figure 6: HCM's expanding oncology commercial team size

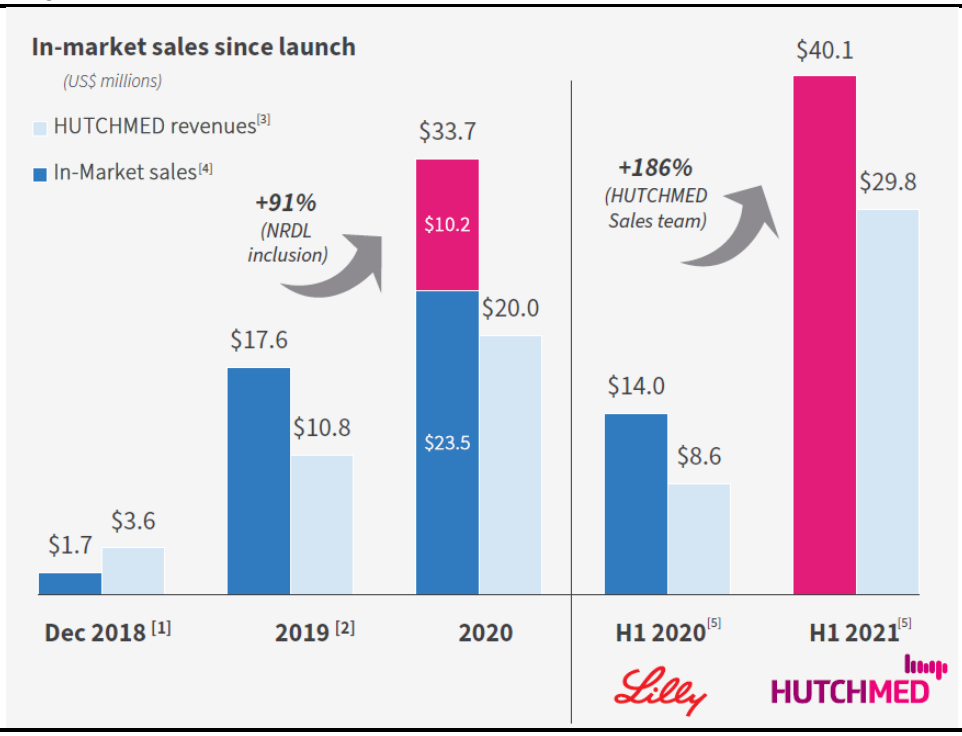


Source: Company data, CMBIS

With deeper hospital coverage, HCM oncology sales team has made instant impact on sales ramp-up of Elunate, after assuming its China commercial responsibility from Eli Lily

in Dec 2020. Elunate's in-market sales surged by 186% YoY to US$40.1mn in 1H21 (vs. US$14.0mn in 1H20).

Figure 7: Elunate sales ramp-up since 4Q20 reflecting HCM's strong commercial capability



Source: Company data, CMBIS

With hematology assets advancing further along the pipeline, build-out of China hematology commercial team is in planning. NDAs of key hematology assets, namely, tazemetostat (EZH2), HMPL-689 (PI3Kδ), HMPL-523 (Syk), and HMPL-306 (IDH1/2) are expected to trigger the scale-up of oncology commercial team in China, in our view.

In the US, HCM is building an oncology commercial team to support potential launches of surufatinib in 2022E and fruquintinib in 2023E.

Expanding in-house manufacturing capabilities

The Company has established a GMP-certified production facility in Suzhou, providing supplies of commercial sales of Elunate and Sulanda, and other drug candidates for clinical trials. To meet the manufacturing demand for upcoming product launches, the Company has commenced construction of a 55,000 m² large-scale manufacturing plant in Shanghai, which is five times that of the existing production site. The first phase will be primarily for small molecule production with expected production capacity of 250mn tablets and capsules per year, whilst the second phase is planned for large molecule drug production.

Figure 8: Expanding manufacturing facility

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

SUZHOU FACTORY

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

SHANGHAI FACTORY

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

Source: Company data, CMBIS

Seasoned management team

HCM is led by an experienced and stable management team of seasoned industry executives, including many with senior-level experience at leading pharmaceutical companies such as Pfizer, Bristol-Myers Squibb, Sanofi, Eli Lilly, Roche and Gilead.

Figure 9: HCM management team

Source: Company data, CMBIS; Note: xx/xx years in industry/at HCM

Christian Hogg, the CEO, joined the Company in 2000 as its first employee. Mr. Hogg has since led all aspects of the creation, implementation and management of strategy, business and listings, including the establishment of both Oncology/Immunology and Other Ventures operations.

Dr. Wei-guo SU (苏慰国), assumed his role as chief scientific officer since Apr 2012. Dr. Su has been leading scientific strategy and responsible for the discovery of all drug candidates within HCM's internal pipeline. Prior to joining HCM in Mar 2005, Dr. Su worked at the US Research and Development department at Pfizer. He was granted the prestigious award by the China Pharmaceutical Innovation and Research Development Association (PhIRDA) as one of the Most Influential Drug R&D Leaders in China.

Savolitinib, first selective MET-inhibitor in China

Approved by the China NMPA in Jun 2021, savolitinib (Orpathys) is the first highly selective oral inhibitor of MET receptor tyrosine kinase (TKI) for treatment of non-small cell lung cancer (NSCLC) patients with MET exon14 skipping alternation in China (occurs in 3-4% NSCLC patients).s

Beyond its approved indication, savolitinib is being assessed in multiple late-stage/registration-intent trials across various cancer types in China and globally, including i) 2L EGFRm+ TKI refractory, MET+ NSCLC in China, ii) Naive EGFRm+, MET+ NSCLC in China), iii) 2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC in the US/EU/Japan, iv) MET+ papillary renal cell carcinoma (PRCC) in the US/EU/Japan, and v) 2L MET+ gastric cancer (GC) in China. Other earlier stage trials under investigation include VEGFR TKI refractory clear cell RCC (ccRCC) in EU and MET+ colorectal cancer (CRC) in the US.

Figure 10: Clinical development plan of savolitinib

Cancer type	Indication	Type of treatment	China status	Global status	Upcoming milestone
NSCLC	MET Exon 14 skipping NSCLC	Mono	Approved in Jun 2021	-	-
	2L EGFRm+ TKI refractory MET+ NSCLC	+Tagrisso	Phase III (in planning)	-	To initiate Phase III trial in 2H21
	Naive EGFRm+ MET+ NSCLC	+Tagrisso	Phase III	-	-
	2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC	+Tagrisso		Global: Phase II	Ongoing; data support progressing into Phase III, expected in 2H21
RCC	MET+ Papillary RCC*	+ IMFINZI	-	Phase III	To begin enrollment in 2H21
	Clear cell RCC (VEGFR TKI refractory) *	+ IMFINZI	-	UK/Spain: Phase II	-
GC	2L+ MET+ GC	Mono	Registration-intent Phase II	-	-
CRC	MET+ mCRC*	Mono	-	US: Phase IIa	-

Source: Company data, CMBIS: Note:* investigator-initiated trials (IIT)

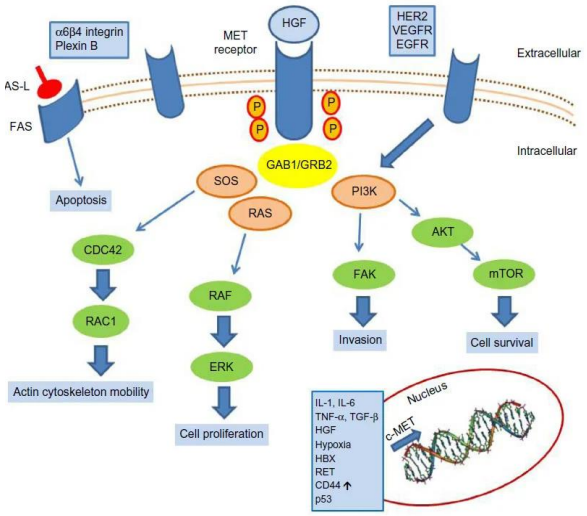
In Dec 2011, HCM granted global development and commercialization rights of savolitinib to AstraZeneca. AstraZeneca paid US$20mn upfront fee and agreed to pay royalties and additional payments upon achievement of development and sales milestone. HCM is responsible for manufacturing while AstraZeneca is responsible for commercialization of savolitinib in China. HCM is entitled to receive 30% fixed royalties on China sales, various development fees, commercial milestones and manufacturing fees paid by AstraZeneca, and up to 14-18% tiered royalties on ex-China sales. HCM and AstraZeneca agreed to share development costs for savolitinib in China while AstraZeneca is responsible for all ex-China development costs.

Mechanism of action of savolitinib

MET is a signalling pathway that has specific roles in normal mammalian growth and development. However, aberrant activation of MET has been demonstrated to be highly correlated in many cancer indications, including kidney, lung, gastric, colorectal, esophageal and brain cancer. It plays a major role in cancer pathogenesis (i.e., development of cancer), including tumor growth, survival, invasion, metastasis, the suppression of cell death as well as tumor angiogenesis.

MET also plays a role in drug resistance in many tumor types. For instance, MET gene amplification has been found in NSCLC and CRC following anti-EGFR treatment, leading to drug resistance. Savolitinib acts by blocking the transduction of downstream c-MET signaling pathway thereby suppressing tumor growth.

Figure 11: Savolitinib inhibits c-MET signalling pathways



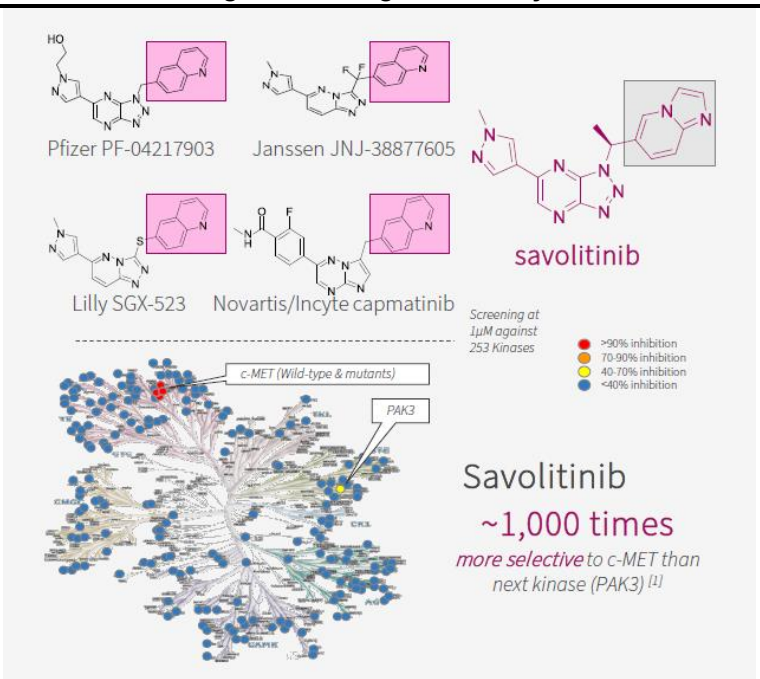
Source: Granito A et al, 2014, CMBIS

Designed with superior c-MET selectivity

Despite a validated therapeutic rationale, development of first-generation c-MET inhibitors have encountered several setbacks mainly due to lack of c-MET selectivity and toxicity tissue. Past trial failures are exemplified by the i) termination of Phase I trial of JNJ-38877605 with the culprit of insoluble metabolite formation causing kidney toxicity, and ii) termination of a Phase III trial of Roche's onartuzumab due to lack of clinically meaningful efficacy in MET+ NSCLC patients.

In pre-clinical trials, savolitinib demonstrated strong in vitro activity against MET, affecting its downstream signaling targets and thus blocking the related cellular functions effectively, including proliferation, migration, invasion, scattering and the secretion of VEGF, that plays a pivotal role in tumor angiogenesis. In the MET enzymatic assay, savolitinib showed potent activity with IC50 of 5 nM. In a kinase selectivity screening with 274 kinases, savolitinib had potent activity against the MET Y1268T mutant (comparable to the wild-type), weaker activity against other MET mutants and almost no activity against all other kinases. Savolitinib was found to be approximately 1,000 times more potent to MET than the next non-MET kinase. Similarly, in cell-based assays measuring activity against MET phosphorylation, savolitinib demonstrated potent activity in both ligand-independent (gene amplified) and ligand-dependent (overexpressed) cells with IC50 at low nanomolar levels. In target related tumor cell function assays, savolitinib showed high potency with IC50 of less than 10 nM. Furthermore, savolitinib demonstrated cytotoxicity only on tumor cells that were MET gene amplified or MET overexpressed. In other cells, inhibition measurements demonstrated that IC50 amounts were over 30,000 nM, which is thousands of times higher than the IC50 on MET tumor cells.

Figure 12: Savolitinib is designed with high selectivity to c-MET



Source: Company data, CMBIS

Comparable clinical data in MET exon 14 skipping NSCLC

MET exon 14 skipping mutation occurs in 3-4% NSCLC patients (Paik P et al, 2020). The approval of savolitinib as monotherapy in patients with MET exon 14 skipping NSCLC was based on a registrational Phase II study in (NCT02897479, n=70). The trial delivered ORR of 42.9% and DCR of 82.9%. With up to 36% patients with pulmonary sarcomatoid carcinoma (PSC), which is a more aggressive NSCLC, trial results showed PFS of 6.8 months (vs 2 months for chemotherapy as standard of care for PSC).

Figure 13: Savolitinib's China registrational Phase II trial data for NSCLC with MET exon 14 alteration

Study	NCT02897479
Trial design	A registrational Phase II, single-arm, open-label, study (N=70)
Indication	NSCLC with MET Exon 14 mutation patients who have failed prior systemic therapy or are unable to receive chemotherapy
Patient profile	36% of patients with PSC
Dosing regime	600mg or 400mg savolitinib administered orally once per day (QD) for 21 days per cycle
Median follow up	17.6 months
Primary endpoint	
ORR	42.9%
DCR	82.9%
Secondary endpoint	
PFS	6.8 months
mOS	12.5 months
Safety data	
Treatment related serious AE	24%
TEAEs (Grade 3 or above)	46%

Source: Company data, Lancet, CMBIS

There are currently two selective C-met inhibitors approved for MET exon 14 skipping NSCLC in the US, namely, Novartis's capmatinib and Merck's tepotinib. We think savolitinib's clinical data are comparable to peers. Nevertheless, we noted that savolitinib's trial had more severe baseline patient profile with up to 36% patients with pulmonary sarcomatoid carcinoma (PSC) which is a more aggressive NSCLC. Under SoC chemotherapy, PSC usually only has an ORR of 16.5%, mPFS of 2 months and mOS of 6.3 months. In contrast, PSC patients only account for 5% of the total enrolled patients in capmatinib's GEOMETRY trial and 1% in tepotinib's vision trial, respectively.

Figure 14: Cross trial comparison of globally approved selective MET inhibitors in MET exon 14 skipping NSCLC

	Savolitinib	Capmatinib		Tepotinib
Company	HCM	Novartis		Merck
Approval year	Jun 2021 (China)	May 2020 (US)		Feb 2021 (US)
Treatment setting	All-comer monotherapy	1L monotherapy	2L/3L monotherapy	1L (44%), 2L/3L (56%) monotherapy
Registrational trial	NCT02897479 (N=70)	GEOMETRY (Cohort 5b) (N=28)	GEOMETRY (Cohort 4) (N=69)	VISION (N=99)
ORR	42.9%	68%	41%	46.5%
DCR	82.9%	96%	78%	65.7%
mDoR	-	12.6 months	9.7 months	11.1 months
mPFS	6.8 months	12.4 months	5.4 months	8.5 months
Grade ≧ 3 TEAE	46%	75% (Grade ≧ 3 AE)	75% (Grade ≧ 3 AE)	28%

Source: Company data, NEJM, CMBIS

Competitive landscape of c-MET inhibitors in MET exon-14 skipping NSCLC

Globally, there are two US FDA approved selective MET inhibitors for the treatment of MET exon-14 skipping NSCLC, namely, Novartis's capmatinib and Merck's tepotinib. According to Fierce Biotech, global peak sales of capmatinib is estimated to reach US$1.5bn.

Figure 15: Approved selective MET inhibitors in the US

Drug	Target	Company	US FDA approval year	Approved indications
Capmatinib	MET	Novartis/Incyte	May 2020	MET exon-14 skipping NSCLC
Tepotinib	MET	Merck	Feb 2021	MET exon-14 skipping NSCLC

Source: F&S, CMBIS

In China, savolitinib is first and only selective small molecule c-MET inhibitor approved for MET exon 14 skipping NSCLC. There are five other selective c-MET inhibitors undergoing late-stage clinical development. Approved by the NMPA in Jun 2021, savolitinib is eligible for the upcoming NRDL revision expected in 3Q21E. We think the potential inclusion in NRDL could pave a solid path for savolitinib's sales ramp-up.

Figure 16: Market landscape of small molecule MET inhibitors in China

Drug	Targets	Company	Drug type	Status	(Targeted) Indications
Savolitinib	MET	HCM/AZ	Original	Approved	MET exon-14 skipping NSCLC
Crizotinib	ALK, MET, ROS1	Pfizer	Original	Approved	ALK+/ROS1+ NSCLC
Capozantinib	VEGFR1/2/3, KIT, TRKB, FLT-3, AXL, RET, MET, TIE-2	Hansoh/Simcere/ Jiangsu Vcare/	Generics	NDA filed/ BE	HCC, RCC

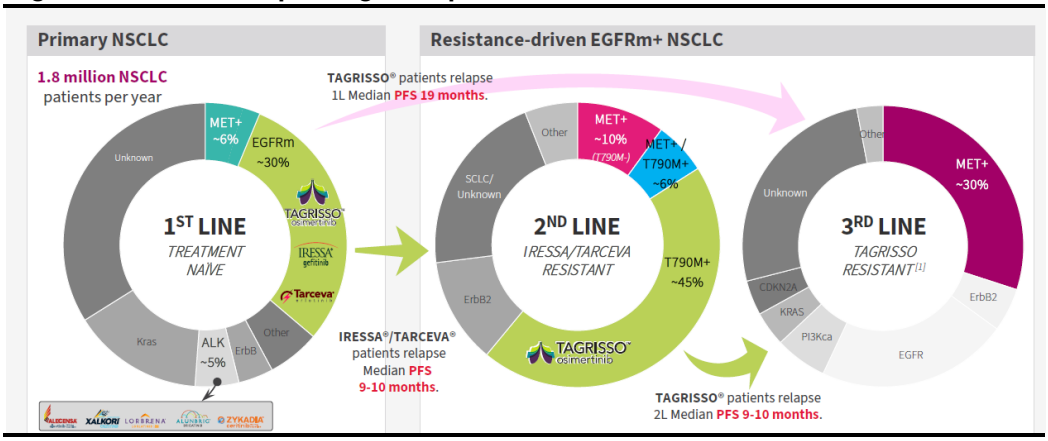
		Jiangsu Aosaikang			
Sitravatinib	MET, RET, TRK	BeiGene	Original	Phase III	NSCLC
Capmatinib	MET	Novartis	Original	Phase II	HCC, EGFR+ NSCLC, MET exon-14 skipping NSCLC, EGFR wild-type/ALK+ NSLCL
Tepotinib	MET	Merck	Original	Phase II	MET+ NSCLC, HCC, EGFR+ NSCLC
Bozitinib	MET	Beijing Pu Run Ao	Original	Phase II	MET+ NSCLC, GBM
Glumetinib	MET	Green Valley Pharma	Original	Phase II	MET+ NSCLC
AL2846	MET	Adenchen	Original	Phase II	NSCLC, bone metastasis, CRC, pancreatic cancer
TQ-B3101	ALK, MET, ROS1	Sino Biopharm	Original	Phase II	ALK+ NSCLC, ALK+ GC, ROS1+ NSCLC, anaplastic large cell lymphoma

Source: Insight, F&S, CMBIS; Note: HCC: hepatocellular carcinoma; RCC: renal cell carcinoma; NSCLC: Non-small cell lung cancer; GBM: glioblastoma

Blockbuster potential in MET+, EGFRm+ NSCLC with Tagrisso sales uptrend

EGFR mutation occurs in 30-40% of NSCLC patients in Asia (vs 10-15% in the US/EU). On treatment paradigm, 1L treatments for EGFRm+ NSCLC patients include 1st-gen EGFR inhibitors such as AstraZeneca's Iressa (gefitinib), Roche's Tarceva (erlotinib), or Tagrisso (osimertinib) if relapsed with 1st-gen EGFR inhibitors, all of which have also been approved in China. Most patients treated with 1st-gen EGFR inhibitors eventually acquire resistance through secondary mutation, with 50% developing T790M mutation which can be treated with Tagrisso as 2L therapy. Overall, approximately 30% of all Targrisso-treated 2/3L EGFRm+NSCLC patients further develop MET aberrations, and therapeutic option for this group of patients (with both MET and EGFR mutation) represents a black hole.

Figure 17: Treatment paradigm for patients with EGFRm+ NSCLC



Source: Company data, CMBIS

Developed by AstraZeneca, Tagrisso has been approved by the US FDA i) as adjuvant therapy for NSCLC with exon 19 deletions/ exon 21 L858R mutations, ii) as the first-line treatment of metastatic NSCLC with EGFR exon 19 deletions/ exon 21 L858R mutations, and iii) as the 2L treatment of metastatic EGFR T790M+ NSCLC.

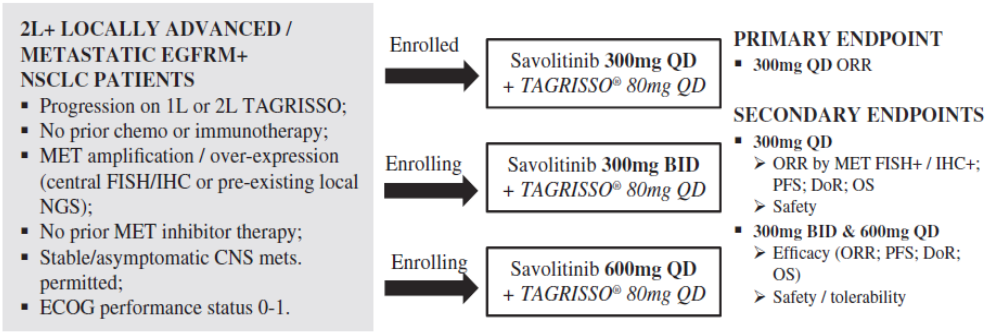
Tagrisso raked in US$4.3bn global sales in 2020 (up 36% YoY), with peak sales estimated to surpass US$8bn in 2025E, according to AstraZeneca. We think savolitinib is poised to unlock its global market potential in MET+, EGFRm+ NSCLC benefiting from the uptrend in Tagrisso sales momentum.

Clinical development plan for MET+, EGFRm+ NSCLC

In China: A Phase III study (SANOVO) of savolitinib in combination with Tagrisso in treatment naïve patients with EGFRm+, MET+ NSCLC has been initiated since Sep 2021. In addition, a Phase III study (SACHI) in combination with Tagrisso in 2L EGFRm+, EGFR TKI refractory, MET+ NSCLC patients is under planning, which is expected to start in 2H21E.

Globally: A global single-arm Phase II trial (SAVANNAH; NCT03778229) is being conducted in combination with Tagrisso as 2L/3L therapy for EGFRm+, MET+ NSCLC patients. The SAVANNAH study has deployed three cohorts with different dosing regimens, with the 300mg QD cohort having fully enrolled while the enrolment for the other two trials (300mg BID and 600mg QD) are still ongoing. SAVANNAH will inform final regulatory, biomarker and dose regimen strategy for the initiation of global Phase III development in late 2021E.

Figure 18: SAVANNAH study design



Source: Company data, CMBIS; Note: EGFRM+ = epidermal growth factor receptor mutation positive; ECOG = Eastern Cooperative Oncology Group; BID = twice daily; QD = once daily; FISH (+) = fluorescence in situ hybridization (positive); IHC (+) = immunohistochemistry (positive); ORR =objective response rate; PFS = progression free survival; DoR = duration of response; OS = overall survival; and MET = mesenchymal epithelial transition receptor.

Unique positioning targeting all-comer PRCC

Kidney cancer is among the top 10 most common cancers worldwide, with an annual incidence of 69,569 in the US in 2020 (Globocan), with renal cell carcinoma (RCC) accounting for 90% of all cases. Clear cell renal cell carcinoma (ccRCC) accounts for 75% of RCC, while papillary RCC (PRCC), a non-ccRCC subtype, accounts for 15% of all RCC (Choueiri T et al, 2020). PRCC is highly driven by MET aberration, which presents in approximately 50% of cases, thus MET-targeted therapeutics represent potential clinical options.

There is an urgent need for PRCC treatment since, so far, none of targeted therapies have approved globally. Pfizer's Sutent (Sunitinib, VEGFR/PDGFR inhibitor) is recommended as SoC treatment for PRCC in both China and the US, as per CSCO/ASCO, despite its low clinical efficacy. Given its first-mover advantage to address the unmet clinical need, we think savolitinib is well positioned to enjoy speedy market penetration globally.

Revamped PRCC combination strategy with Imfinzi, on the basis of SAVOIR and CALYPSO study

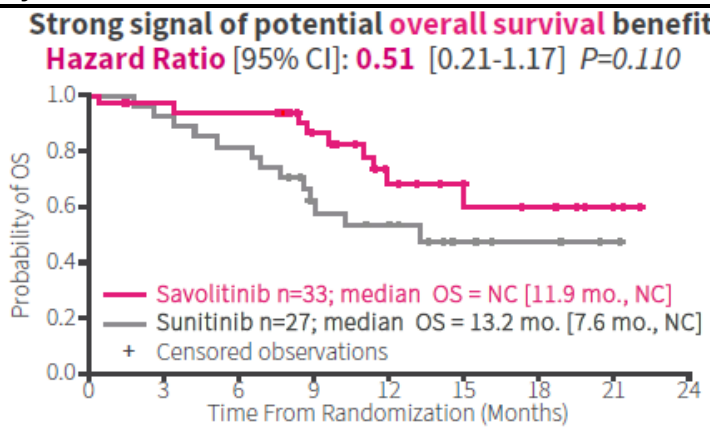
SAVOIR study (NCT03091192): An open-label, randomized controlled Phase III study (SAVOIR) was first initiated in Jun 2017, evaluating savolitinib as monotherapy in MET-driven PRCC vs Sutent. The trial was terminated in Dec 2018 due to confounding results of an external epidemiology study indicating that patients with MET-driven PRCC responded indifferently to Sutent compared to those without MET. Although the primary endpoint of PFS failed to achieve statistical significance (vs the Sutent arm), all efficacy measures of PFS, OS and ORR were numerically greater with savolitinib in 60 evaluated patients as of cut-off date in Aug 2019. In particular, the study demonstrated a strong signal of response and potential survival benefit with OS was not reached in savolitinib arm vs 13.2 month in Sutent arm with a hazard ratio of 0.51. Moreover, savolitinib is associated with superior safety profile with less incidence of both Grade ≥ 3 AEs and AEs leading to dose modification.ss

Figure 19: SAVOIR study comparing savolitinib with Sutent in MET-driven PRCC

	SAVOIR (NCT03091192)
Trial design	A global Phase III, open-label, randomized, controlled trial evaluating the efficacy and safety of savolitinib as monotherapy vs Sutent (1:1)
n	60 (as of cut-off date of Aug 2019)
Indication	All-comer MET+ PRCC
Dosing regime	600 mg once daily
Primary endpoint	
PFS	7 months vs 5.6 months (HR = 0.71)
Secondary endpoint	
ORR	27.3% vs 7.4%
OS	Not reached vs 13.2 month
Safety data	
Grade ≧ 3 or above AE	42% vs 81%
AE leading to dose modification	30% vs 74%

Source: Company data, CMBIS

Figure 20: Savolitinib demonstrated strong signal of potential OS benefit in SAVOIR study



Source: Company data, CMBIS

CALYPSO study (NCT02819596**):** A UK/Spain-based Phase II trial (CALYPSO) of savolitinib in combination with Imfinzi is ongoing in patients with PRCC and VEGFR TKI

refractory clear cell RCC. According to interim results of CALYPSO's PRCC cohort presented at 2021 ASCO, savolitinib showed encouraging efficacy regardless of PD-L1 or MET status. Among the 41 patients regardless of PD-L1 or MET status, ORR was 29% while mPFS was 4.9 months. For the 14 MET-driven patients, ORR was 57%, while mPFS was 10.5 months and mOS was 27.4 months.

Figure 21: Interim results of PRCC cohort of CALYPSO study presented at 2021 ASCO

PRCC cohort of CALYPSO Study	All patients	MET-driven PRCC
n	41	14
ORR	29%	57%
mPFS	4.9 months	10.5 months
mOS	14.1 months	27.4 months
PFS at 12 months	29.6%	46.2%
OS at 12 months	54.3%	65.4%

Source: Company data, CMBIS

Based on compelling clinical results from the SAVOIR and CALYPSO study, HCM and AstraZeneca plan to initiate a global phase III, open-label, randomized controlled study (SAMETA) of savolitinib in combination with Imfinzi (vs sunitinib monotherapy and vs Imfinzi monotherapy) in patients with MET+ PRCC, which is expected to commence in 2H21E.

Additional label expansion opportunities

Given the wide association of MET aberration across various cancer types, savolitinib is also being investigated in gastric cancer (GC) in China and colorectal cancer (CRC) in the US.

Figure 22: MET aberration occur in different tumor settings

		MET		2020 New cases	
Indication	Amplification	Mutation	Over-Expression	China	Global
Gastric	10%	1%	41%	469,600	1,089,100
NSCLC	4%/16%/30%	2%	39%	785,500	1,875,800
Head & Neck	17-39%	11%	46%	143,100	931,900
Colorectal	10%	3%	65%	453,400	1,880,700
Papillary RCC	64%	70-100%	55%	3,839	48,500
Clear Cell RCC	54%	NA	35%	60,030	300,900
Esophagus	8%	NA	92%	289,600	604,100
Prostate	NA	NA	54/83%	114,300	1,414,300

Source: Company data, F&S, CMBIS

GC in China: GC is the fourth most prevalent cancer in China, with annual incidence of 478,508 in 2020 (Globocan). MET amplification occurs in 4-6% of GC patients (Lee J et al 2019). The Company has initiated a single-arm registration-intent Phase II trial of savolitinib monotherapy as 2L or above treatment for MET-amplified GC patients in China, with the first patient dosed in Jul 2021.

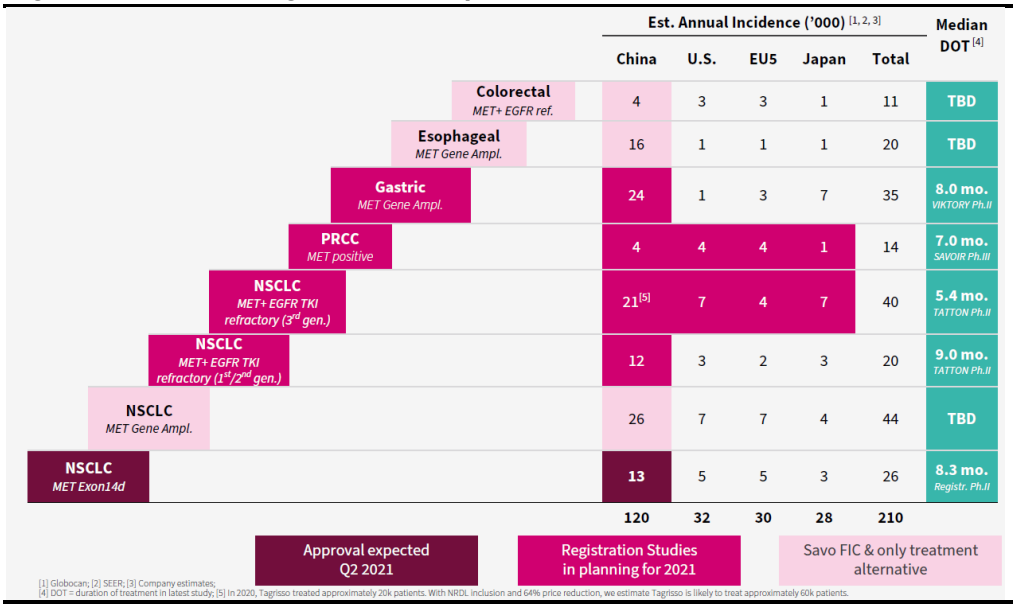
CRC in the US: CRC is the fourth most prevent cancer in the US, with annual incidence of 155,008 in 2020 (Globocan). MET amplification occurs in 10% CRC patients, while 65% have MET overexpression. Sponsored by National Cancer Institute, a single-arm phase II

trial of savolitinib monotherapy as 2L or above treatment for mCRC (NCT03592641) is ongoing with a plan to enroll approximately 15 MET amplified CRC patients in the US.

Market opportunity of savolitinib

As of 2030E, for exon 14 skipping NSCLC, we model sales of US$166mn in China, with US$72mn in revenue attributable to HCM. We view the key to unleashing its market potential largely hinges on label expansion opportunities in: i) 2L EGFRm+ TKI refractory MET+ NSCLC in China, ii) naive EGFRm+ MET+ NSCLC in China, iii) 2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC in the US/EU/Japan, and iv) 2L MET+ GC in China, with estimated market launch in 2024E, respectively. Overall, we model risk-adjusted global sales of US$1.08bn for savolitinib with US$322mn in revenue attributable to HCM in 2030E, and risk-adjusted global peak sales of US$1.18bn with US$348mn in revenue attributable to HCM in 2033E.

Figure 23: Savolitinib global market potential



Source: Company data, CMBIS

Figure 24: Savolitinib revenue build summary

Market	Indications	Targeted patient population	Patients treated with savolitinib	(Expected) year of launch	Probability of success	Risk-adjusted sales in 2030E (US$ mn)	% of HCM attributable revenue	HCM attributable revenue in 2030E (US$ mn)
China	MET exon14 skipping NSCLC	24,136	13,757	2021	-	166	43%	72
	2L EGFRm+ TKI refractory MET+ NSCLC	19,308	9,654	2024	80%	105	43%	45
	EGFRm+, MET+ Naive NSCLC	24,136	10,378	2024	80%	113	43%	49
	2L+MET+GC	27,766	13,050	2024	80%	126	43%	54
US	2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC	8,092	3,399	2024	80%	156	18%	28
	MET+ PRCC	4,905	2,207	2024	80%	129	18%	23
EU/Japan	2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC	8,092	3,399	2024	80%	156	18%	28
	MET+ PRCC	4,905	3,399	2024	80%	129	18%	23
Total						**1,080**		**322**

Source: Company data, CMBIS estimates

Surufatinib, dual-target of tumor angiogenesis and immune invasion with board applicability

Surufatinib (brand name: Sulanda) is a novel, oral small molecule tyrosine kinase inhibitor (TKI) targeting VEGFR/FGFR/CSF-1R kinases, approved by the China NMPA for patients with grade 1/2 non-pancreatic neuroendocrine tumors (npNET) and pancreatic NET (pNET) in Dec 2020/Jun 2021, respectively. Globally, NDA submission to the US FDA and MAA filing to the EU EMA for NETs were both accepted in Jul 2021. Beyond NETs, surufatinib is also being assessed in various solid tumors as monotherapy or combination therapy with Junshi's toripalimab (PD-1) and BeiGene's tislelizumab (PD-1) both in China and globally. HCM owns global rights of surufatinib which is currently being marketed by HCM's in-house oncology commercial team in China.

Figure 25: Clinical development plan of surufatinib

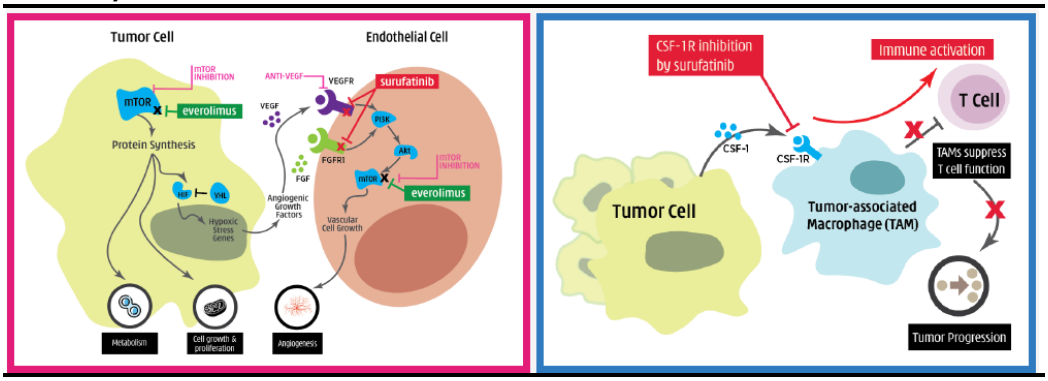
Indication	Type of treatment	China status	Global status	Upcoming event
Non-pancreatic NET	Mono	Approved in Dec 2020	-	-
Pancreatic NET	Mono	Approved in Jun 2021	-	-
NETs, BTC and soft tissue sarcoma	Mono	-	**NETs:** NDA accepted by US FDA in Jul 2021; MAA accepted by EMA in Jul 2021; **BTC, STC**: Phase Ib (US/EU) ongoing	-
2L Biliary tract cancer	Mono	Phase IIb completed	-	Priority for PD-1 mAb combo for future BTC development
Solid tumors (NENs, BTC, GC, thyroid cancer, SCLC, STS endometrial cancer, esophageal cancer, NSCLC)	+ Toripalimab	Phase II	-	**NEC**: to initiate Phase III trial in 2H21; **GC:** registration design under discussion
Solid tumors	+ Sintilimab	Phase I	-	-
Solid tumors (CRC, NET, SCLC, GC, STS)	+Tislelizumab	-	US/EU: Phase Ib/II	-

Source: Company data, CMBIS; Note: BTC: Biliary tract carcinoma; SCLC: small cell lung cancer; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma, GC: gastric cancer

Mechanism of action of surufatinib

Both vascular endothelial growth factor receptor (VEGFR) and fibroblast growth factor receptor (FGFR) signaling pathways play a role in mediating tumor angiogenesis, whilst colony stimulating factor 1 receptor (CSF-1R) is key in facilitating the production tumor-associated macrophage that promotes tumor growth and metastasis. Blockage of VEGFR, FGFR1 and CSF1R kinases hence leads to inhibition of tumor angiogenesis and tumor immune evasion.

Figure 26: Differentiated mechanism of action of surufatinib vs everolimus (mTOR inhibitor)



Source: Company data, CMBIS

Broad patient eligibility for all types of NETs is a key differentiator

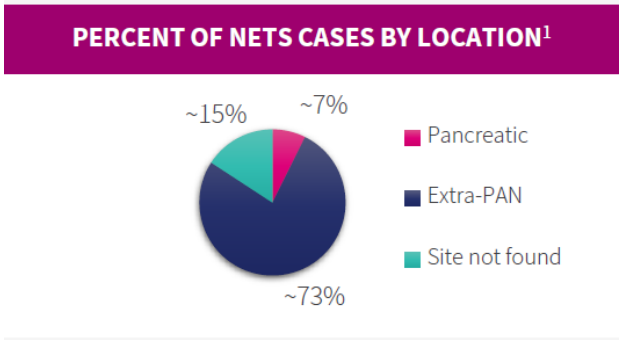
NETs disease profile

NETs are types of tumors that originate from neuroendocrine cells localized in different organs throughout the body. Among all organ origins, NETs are commonly found in gastrointestinal system such as small intestine (30.8%), rectum (26.3%), colon (17.6%), pancreas (12.1%), and appendix (5.7%), and in the lung (25.7%), according to American Cancer Society. NETs can be classified as pancreatic NETs (NETs originated from pancreas) and non-pancreatic NETs (originated from the rest of body). Alternatively, NETs can also be categorized into “functional NETs” characterized by hypersecretion of hormones from tumor that result in clinical symptoms (approximately 30% of cases), and “non-functional NETs” without hormones secretion nor symptoms (70% of cases).

NETs treatment paradigm

Surgery is the 1L treatment for localized NETs. However, the majority of patients do not suit for surgical treatment at advanced stages. For advanced G1/G2 NETs, treatments include somatostatin analogues (SSAs) such as octreotide and ianreotide, chemotherapy, radiotherapy such as peptide receptor radionuclide therapy (PRRT), and targeted therapy such as Novartis’s everolimus (mTOR inhibitor) and Pfizer’s sunitinib (tyrosine kinase inhibitor), according to ESMO and 2020 Chinese guidelines for the diagnosis and treatment of pancreatic neuroendocrine neoplasm (pNET).

Figure 27: Classification of NET cases by location



Source: Company data, CMBIS

Figure 28: NET treatment paradigm

Source: Company data, CMBIS

However, none of the aforementioned therapies can treat all types of NETs. Everolimus has only been approved for treating pNET and non-functional GI/lung NET, whereas sunitinib has only been approved for pNET. Surufatinib is well poised to close the therapeutic gap of all types of advanced NETs.

Figure 29: NET treatment landscape in China and the US

Drug class	Somatostatin-based therapies			Kinase inhibitor therapies		
Drug name	Sandostatin LAR (octreotide)	Somatuline Depot (lanreotide)	Lutathera (177Lu-Dotatate)	Affinitor (everolimus)	Sutent (sunitinib)	Sulanda (Surufatinib)
Company	Novartis	Ipsen	Novartis	Novartis	Pfizer	HCM
MOA	Somatostatin analogue	Somatostatin analogue	Somatostatin analogue targeting radiotherapy	mTOR inhibitor	Multiple RTK inhibitor	VEGFR/FGFR1 & CSF-1R inhibitor
Administration route	Subcut/intra-muscular injection	Subcut injection	IV injection (radio-qualified physicians)	Oral tablet	Oral capsule	Oral capsule
Approved NET Indications	Long term treatment of severe diarrhea and flushing from metastatic carcinoid tumors	Gastroenteropancreatic NETs to improve PFS; Carcinoid Syndrome to reduce frequency of short-acting somatostatin rescue therapy	Somatostatin receptor+ GEP-NETs	pNET; non-functional GI or Lung NET	pNET	pNET& non-pNET
US approval	Yes	Yes	Yes	Yes	Yes	NDA filed
China approval	Yes	Yes	No	Yes	Yes	Yes
2020 US sales (US$)	$1.4bn	$1.5bn	$0.4bn	$1.1bn	$0.8bn	N/A

Source: Company data, CMBIS

Surufatinib showed compelling clinical evidence for pNET and non-pNET

The NMPA's approval of surufatinib as 1L/2L treatment for grade 1 and grade 2 non-pancreatic NETs in Dec 2020 was based on the interim analysis of Phase III trial (SANET-ep) as of data cut-off time in mid-2019. The trial met its pre-defined primary endpoint of PFS, and hence terminated early. The trial yielded robust efficacy data with PFS of 9.2 months (vs. 3.8 months for the control group) with a hazard ratio of 0.33. Surufatinib was well tolerated, with grade ≥3 TEAEs including hypertension (36% of incidence), proteinuria (19%) and anemia (7%).

Figure 30: Surufatinib's China Phase III trial data for non-pancreatic NETs

Study	SANET-ep (NCT02588170)
Trial design	A randomized, double-blind, placebo controlled, multi-center Phase III trial (n=198)
Dosing regimen	300 mg surufatinib QD, orally administrated on a 28-day cycle
Patient eligibility	Patients with grade 1/2 non-pancreatic NETs that have previously received no more than two types of therapies
Primary endpoint	PFS
Secondary endpoints	ORR, DCR, TTR, DoR, OS and safety and tolerability
Median follow up	13.8 months
Efficacy data	
PFS	9.2 months vs. 3.8 months; HR: 0.33
Safety data	
TEAEs (grade ≥3)	Hypertension: 36% vs.13%; Proteinuria: 19% vs. 0%
Treatment-related serious adverse events	25% vs.13%
Treatment-related deaths	3 patients vs.1 patient

Source: Company data, Lancet, CMBIS; Note: ORR: objective response rate; DCR: disease control rate; DoR: duration of Response; TTR: Time to Response; OS: overall survival

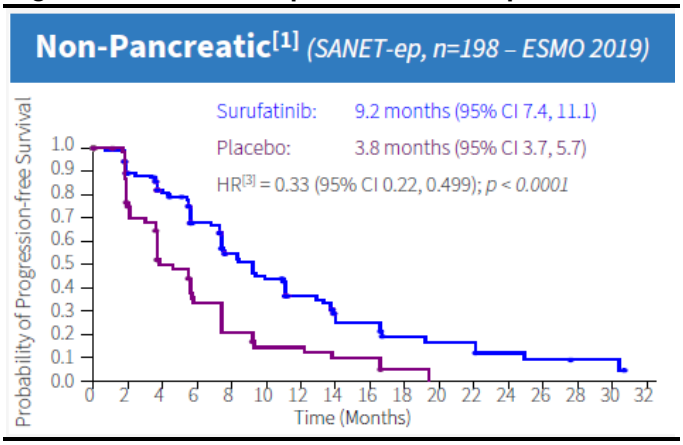
The NMPA's approval of surufatinib for the treatment for grade 1 and grade 2 pNETs in Jun 2021, was on the basis of the interim analysis of Phase III trial (SANET-p) as of data cut-off time in early 2020. The trial met its pre-defined primary endpoint of PFS, and thus stopped early. The trial yielded compelling efficacy data with PFS of 10.9 months (vs. 3.7 months for the control group) with a hazard ratio of 0.49. ORR was 19.2% for surufatinib-treated patients (vs.1.9% for the placebo). DCR was 88.8% (vs. 66.0% for the placebo). Surufatinib was well tolerated for most patients, with discontinuation rates due to TEAEs of 10.6% (vs. 6.8% in the control group).

Figure 31: Surufatinib's China Phase III trial data for pancreatic NETs

Study	SANET-p (NCT02589821)
Trial design	A randomized, double-blind, placebo controlled, multi-center Phase III (n=172)
Dosing regimen	300 mg surufatinib QD, orally administrated on a 28-day cycle
Patient eligibility	Patients with grade 1/2 non-pancreatic NETs that have previously received no more than two types of therapies
Primary endpoint	PFS
PFS	10.9 months vs. 3.7 months (placebo); HR: 0.49
Secondary endpoint	ORR, DCR, TTR, DoR, OS and safety and tolerability
ORR	19.2% vs. 1.9%
DCR	80.8% vs. 66.0%
Median follow up	19.3 months
Safety data	
TEAEs (grade ≥3)	Hypertension: 38% vs. 7%; Proteinura: 10% vs. 2%; Hypertriglyceridemia 7% vs. 0%
Treatment-related serious adverse events	22% vs. 7%
On-treatment deaths	3 deaths (2 due to adverse events, 1 due to disease progression) vs. 1 death (due to disease progression)

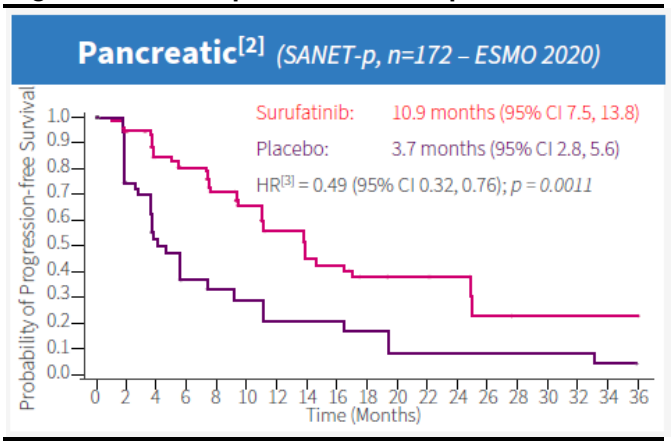
Source: Company data, Lancet, CMBIS; Note: ORR: objective response rate; DCR: disease control rate; DoR: duration of Response; TTR: Time to Response; OS: overall survival

Figure 32: PFS in non-pancreatic NETs patients



Source: Company data, CMBIS

Figure 33: PFS in pancreatic NETs patients



Source: Company data, CMBIS

We compared pivotal trial data among surufatinib, everolimus and sunitinib, given all of which are indicated for grade 1/2 pancreatic NET in front-line settings, although usual caveats of cross trial comparison may apply. Results of surufatinib's pivotal trial showed numerically greater ORR (19%), compared to that of everolimus (5%) and sunitinib (9%).

Figure 34: Cross-trial comparison of surufatinib (vs everolimus and sunitinib)

	Affinitor (everolimus)		Sutent (sunitinib)	Sulanda (surufatinib)	
Indication	pNET	Lung & GI NET	pNET	pNET	non-pNET
Pivotal trial	RADIANT-3	RADIANT-4	A6181111	SANET-p	SANET-ep
mPFS	11.0 months / 4.6 months (HR:0.34, P<0.001)	11.0 months / 3.9 months (HR:0.48, P<0.001)	11.4 months / 5.5 months (HR:0.42, P<0.001)	10.9 months / 3.7 months (HR:0.49, P=0.0011)	9.2 months / 3.8 months (HR:0.3, P<0.0001)
ORR	5% / 2%	2% / 1%	9% / 0%	19% / 2%	10% / 0%
DCR	73% / 51%	81% / 64%	72% / 60%	81% / 66%	87% / 66%

Source: Company data, Lancet, CMBIS

Globally, surufatinib's NDA submission to the US FDA and MAA filing to the EU EMA for treating NETs were both accepted in Jul 2021, respectively. The filings were based on results from Phase III SANET-ep and SANET-p studies conducted in China, along with results from the ongoing US Phase Ib trial (NCT02549937) in patients with epNET and pNET. The US FDA has granted surufatinib Organ Drug Designation for pNETs in Nov 2019 and Fast Track Designation for both pNET and npNET in Apr 2020.

Combination strategy with PD-1 to further unlock clinical value

Surufatinib, through CSF-1R blockage, can interfere with the proliferation and survival of TAM (which promotes angiogenesis and immunosuppression), thereby amplifying anti-tumor activity of PD-1 mAbs. HCM strategically deployed combination approaches with Junshi's Tuoyi (toripalimab/PD-1 mAb) across nine indications, including neuroendocrine carcinoma (NEC), biliary tract carcinoma (BTC), GC, thyroid cancer, SCLC, soft tissue sarcoma, endometrial cancer, esophageal cancer and NSCLC. In addition, the Company

also adopted combination approach with Innovent's Tyvyt (sintilimab/PD-1 mAb) for solid tumors in China and with BeiGene's Baize'an (tislelizumab/PD-1 mAb) for solid tumors targeting ex-China market.

Figure 35: Surufatinib's PD-1 combination study Summary

PD-1	Partner	Indication	Trial location	Status/development plan
Tuoyi (toripalimab)	Junshi	NEC BTC Gastric cancer Thyroid cancer SCLC Soft tissue sarcoma Endometrial carcinoma Esophageal cancer NSCLC	China	Phase II going; **2L+NEC:** to initiate Phase III trial in 2H21; **GC**: Registration design under discussion
Tyvyt (sintilimab)	Innovent	Solid tumors	China	Phase I ongoing
Baize'an (tislelizumab)	BeiGene	Solid tumors (CRC, NET, SCLC, GC, STS)	US/EU	PhaseIb/II ongoing

Source: Company data, CMBIS; Notes: BTC: Biliary tract carcinoma; SCLC: small cell lung cancer; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma

Surufatinib (combo with Tuoyi) in NEC to enter into Phase III trial in China in 2H21E. A single arm, open-label, multicenter, Phase II trial (NCT04169672) of surufatinib in combination with toripalimab is ongoing in China, exploring nine solid tumor indications. At ASCO 2021, encouraging preliminary data were disclosed for the surufatinib and Tuoyi combination in the NEC and gastric cancer cohorts. For the 20 patients in the NEC cohort who received an average of 5 cycles of treatments and are efficacy evaluable, ORR was 20% while DCR was 70%. Median PFS was 3.9 months (95% CI: 1.3-NR). Grade 3 or higher TRAEs occurred in 33% of patients. Moreover, median duration of treatment for the gastric cancer cohort was 3 months, with 15 efficacy evaluable patients at the time of the analysis. For these 15 patients, confirmed ORR was 13% and an additional 20% of patients had unconfirmed response. DCR was 73% and median PFS was 3.7 months (95% CI: 1.4-NR). Grade 3 or higher TRAEs occurred in 14% of patients. HCM plans to prioritize and initiate a Phase III combo study for NEC in 2H21E and registration design for gastric cancer is under discussion.

Adopting a combination approach for BTC in China. A randomized, open-label, active-control Phase IIb/III trial (NCT03873532) is ongoing evaluating surufatinibs monotherapy (vs capecitabine) for 2L BTC in China. Enrollment for the Phase IIb portion (80 patients) of this study was completed in late 2020. Based on the emerging data from our Phase II cohort of the surufatinib combination plus Tuoyi in BTC (NCT04169672), HCM is now prioritizing the combination over surufatinib monotherapy for further development.

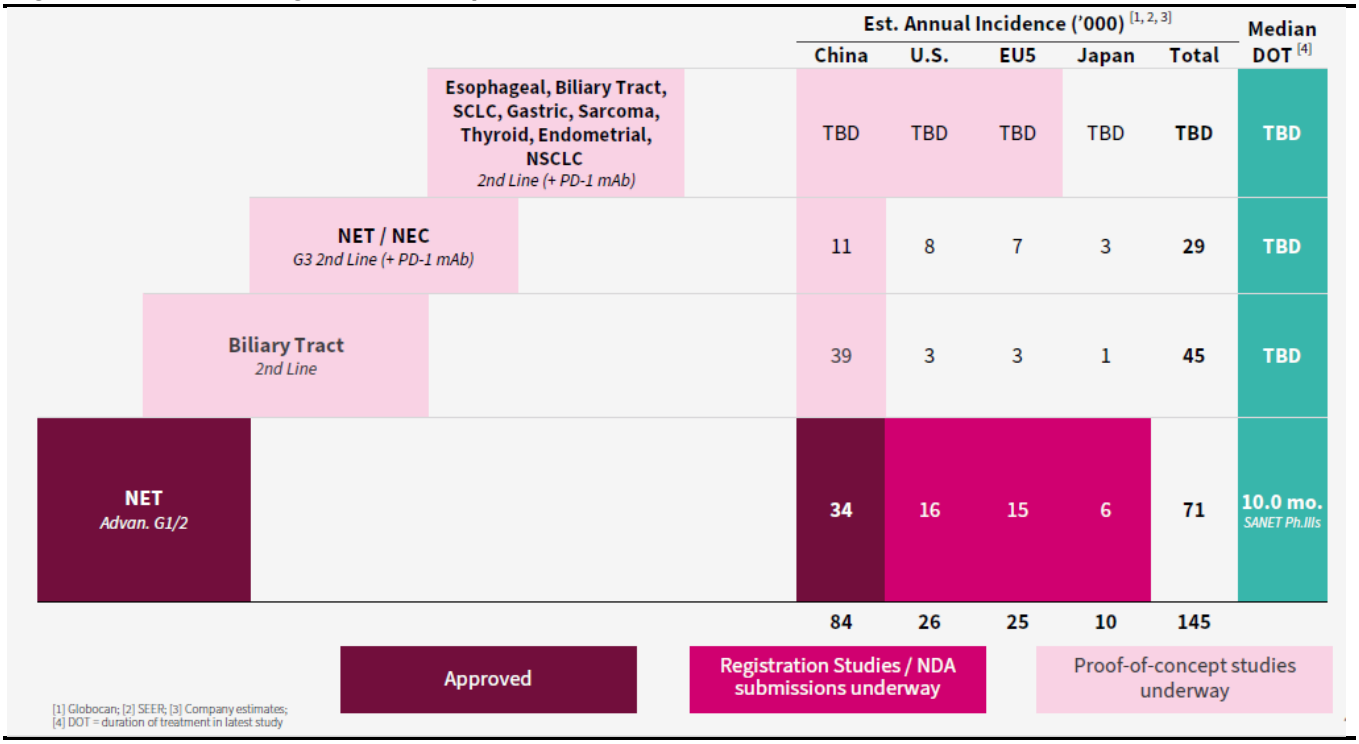
Multiple solid tumors under Phase Ib/II investigation globally. The Company is conducting a Phase Ib/II trial (NCT04579757) in combination with tislelizumab for various solid tumors (including CRC, NET, SCLC, GC, and soft tissue sarcoma) in the US/EU, with the first patient being dosed in Mar 2021.

Market opportunity of surufatinib

As of 2030E, for npNET and pNET, we model respective sales of US$23mn/US$116mn in China. For NETs in the US/EU, we project market launch in 2022E and model risk-

adjusted sales of US$525mn in ex-China market in 2030E. We also estimate risk-adjusted sales of US$314mn in 2030E for surufatinib's combination trials with Junshi's toripalimab across nine solid tumor indications, after factoring in potential launch timelines in 2024E/2025E, treatment landscape for each indication and PD-1's penetration in 2L setting in China. Overall, we forecast surufatinib to generate risk-adjusted global sales of US$978mn in 2030E, and risk-adjusted global peak sales of US$1.00bn in 2032E.

Figure 36: Surufatinib global market potential



Source: Company data, CMBIS

Figure 37: Surufatinib revenue build summary

Indication	Targeted patient population	Patients treated with surufatinib	(Expected) year of launch	Probability of success	Risk-adjusted sales in 2030E (US$ mn)
npNET (China)	5,809	3,195	Approved in Dec 2020	-	23
pNET (China)	39,702	16,119	Approved in Jun 2021	-	116
NET (US)	13,515	3,379	2022	95%	263
NET (EU)	13,515	3,379	2022	95%	263
Various solid tumors combo with PD-1mAb (China)	383,000	107,240	2024/2025	80%	314
Total					**978**

Source: Company data, CMBIS estimates

Fruquintinib, a uniquely selective VEGFR 1/2/3 inhibitor

Fruquintinib (brand name: Elunate) is a novel anti-VEGFR 1/2/3 tyrosine kinase inhibitor (TKI), approved by the China NMPA in Sep 2018, as 3L treatment for advanced colorectal cancer (CRC). It has been included in NRDL since Jan 2020. Fruquintinib recorded in-market sales of US$33.7mn/US$40.1mn in 2020/1H21, up 91.5%/186% YoY respectively. With China' rights out-licensed to Eli Lily in Oct 2013, Elunate had been commercialized by Eli Lily until Oct 2020 when HCM assumed its commercial responsibility. HCM retains ex-China rights, and is entitled to receive 70%-80% of Elunate China sales in form of royalties, manufacturing cost and additional service payments sfrom Eli Lily.

Figure 38: Clinical development plan of fruquintinib

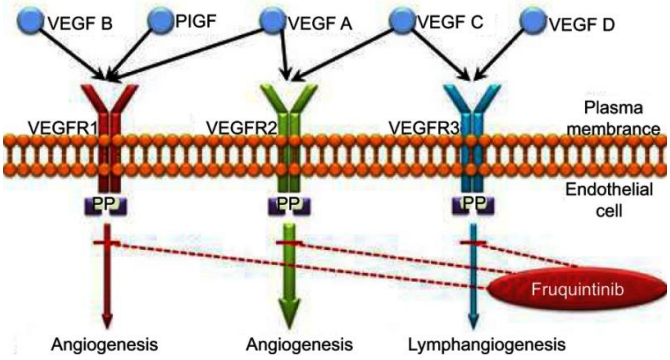
Indication	Regimen	China status	Global status	Upcoming event
3L CRC	Mono	Approved in Sep 2018	-	-
2L CRC	Mono	-	US/EU/Japan: Phase III	To complete Phase III patient enrollment by late 2021E
CRC, TNBC, HR+/HER2- breast cancer	Mono	-	US: Phase Ib	-
2L GC	+ Paclitaxel	Phase III	-	To complete Phase III patient enrollment by 2021E, topline data expected in 2H22E, NDA submission expected in 2022E
HCC, endometrial cancer, RCC and GI tumors	+ Sintilimab	Phase II	-	To initiate Phase III trial in 2H21E in EMC
CRC	+ Sintilimab	Phase II	-	-
CRC	+ Geptanolimab	Phase Ib	-	-
NSCLC	+ Geptanolimab	Phase Ib	-	-
TNBC	+ Tislelizumab	-	Phase Ib/II	-
Solid tumors (GC, CRC and NSCLC)	+ Tislelizumab	-	Korea/China: Phase Ib/II	-

Source: Company data, CMBIS; Note: TNBC: triple negative breast cancer; CRC: colorectal cancer; HCC: hepatocellular carcinoma; GI: gastrointestinal cancer; NSCLC: non-small cell Lung cancer; RCC: renal cell carcinoma

Mechanism of action of fruquintinib

Tumors at advanced stage can secrete large amounts of vascular endothelial growth factor (VEGF), a protein ligand, of which the binding to VEGF receptors stimulate angiogenesis (formation of excessive blood vessels around the tumor as such to provide greater blood flow, oxygen, and nutrients to support tumor growth. By blocking the VEGF/VEGFR signalling pathway, fruquintinib can inhibit angiogenesis and thereby stop tumor development.

Figure 39: Fruquintinib's mechanism of action

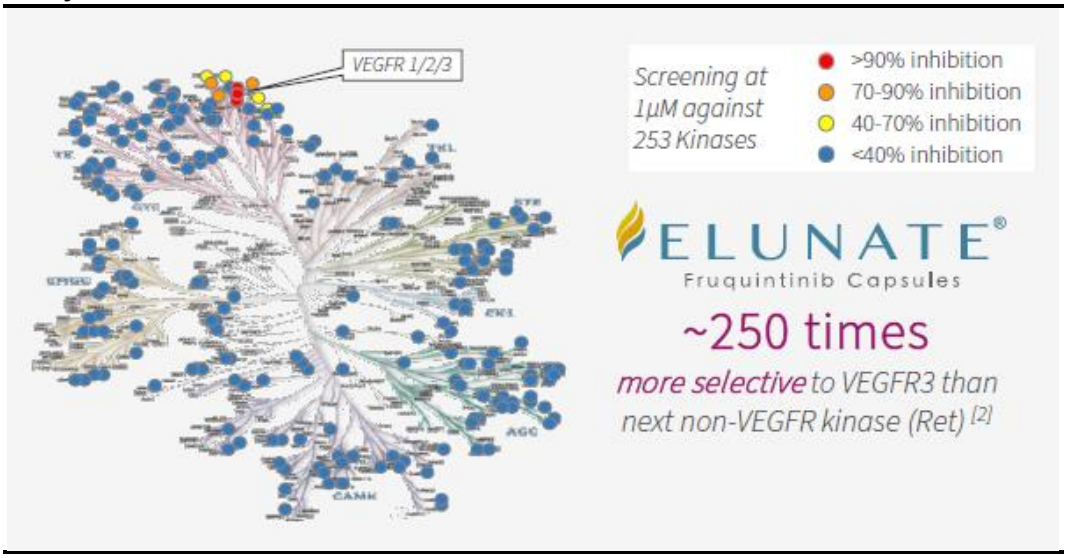


Source: Zhang Y et al, 2019, CMBIS

Optimized clinical profile with high selectivity

Anti-VEGF therapies represents one of the major drug classes across multiple oncology indications. Compared to existing ones that tend to be more selective to VEGFR 1 and 2, Elunate was found to also exert high selectivity against VEGFR3 (approximately 250 times more selective to VEGFR 3 than to non-VEGFR kinase), which plays a major role in lymph-angiogenesis and thereby synergistically inhibits tumor growth.

Figure 40: Fruquintinib showed high potency against VEGFR1/2/3 in pre-clinical study



Source: Company data, CMBIS

Moreover, Elunate showed minimized off-target side effect due to limited or no interaction with other kinases, preventing the activation of kinase-induced downstream signaling pathway. With optimized and clean selectivity profile, Elunate provides strong basis for future strategy with other therapeutics, including internal pipeline assets such as Tazeverik (tazemetostat/ EZH2 inhibitor).

Figure 41: Fruquintinib showed high selectivity against VEGFR3 and minimized off-target effect (vs other anti-VEGF therapies) in pre-clinical study

	1st Generation		2nd Generation			Next Generation
Selectivity	Multiple targets		Relatively selective			Highly selective
Drug	Sutent (Sunitinib)	Nexava (Sorafenib)	Fotivda (Tivozanib)	Lenvim (Lenvatinib)	Inlyta (Axitinib)	Elunate (Fruquintinib)
Company	Pfizer	Bayer	Aveo Oncology	Eisai	Pfizer	HCM
VEGFR1 (nM)	2	26	30	22	3	33
VEGFR2 (nM)	9	90	6.5	4	7	25
VEGFR3 (nM)	19	20	15	5	1	0.5
Phos-KDR (nM)	10	30	0.16	0.8	0.2	0.6
Other kinases (IC50 < 100nM)	PDGFRα PDGFRβ c-Kit Flt3 Ret CSF-1R	Raf-1 b-raf Flt3 P38 c-Kit Ret	PDGFRα PDGFRβ EphB2 c-Kit Tie2	PDGFRα PDGFRβ FGFR1-4 Ret c-Kit	PDGFRα PDGFRβ c-Kit	None

Source: Company data, CMBIS

The approval of fruquintinib for 3L CRC was based on a randomized, double-blind, placebo-controlled, multi-center Phase III trial (NCT02314819) in China. The primary endpoint of median OS was 9.3 months in patients treated with fruquintinib, compared to 6.6 months for the control group, with a hazard ratio (HR) of 0.65. The secondary endpoint of median PFS was 3.7 months, compared to 1.8 months in the control group with HR of 0.26. Other secondary endpoints also demonstrated significant benefits, with disease control rate and ORR of 62% and 5% for the fruquintinib arm, respectively (vs. 12% and 0% for the placebo).

Figure 42: Fruquintinib's Phase III trial data for 3L CRC

Study	FRESCO (NCT02314819)
Trial design	A randomized, double-blind, placebo-controlled, multi-center, Phase III trial (n=416)
Dosing regimen	5mg fruquintinib orally administered once daily for 21 days, followed by 7 days off in a 28-day cycle
Patient eligibility	mCRC patients who failed at least two prior systemic antineoplastic therapies, including Fluoropyrimidine, Eloxatin and Camptosar
Median follow up	13.3 months
Primary endpoint	
Median OS	9.30 months vs 6.57 months (HR: 0.65)
Secondary endpoint	
PFS	3.71 months vs 1.84 months (HR: 0.26)
DCR	62.2% vs.12.3%
ORR	4.7% vs. 0%
Safety data	
All TEAEs	98.6% vs. 88.3%
TEAEs (grade ≥3)	61.2% vs. 19.7%
Treatment-related serious adverse event	6.1% vs. 1.5%
Treatment-related serious adverse event leading to drug continuation	15.1% vs. 5.8%

Source: Company data, JAMA, CMBIS

Fruquintinib's clinical profile looks competitive, compared to its key competitor Bayer's Stivarga (regorafenib), which is also recommended as 3L treatment for CRC in China. While it is difficult to directly evaluate and compare clinical results across separate trials, fruquintinib's efficacy data from its registrational FRESCO study compared favourably to Stivarga's data from CONCUR study conducted in Asia and the global CORRECT study, in our view. On safety, fruquintinib showed more favourable safety profile with lower off-target toxicities, hepatotoxicity and tolerability, compared to Stivarga. Stivarga was approved with a black box warning for liver toxicity on its FDA label. We highlight a noticeable difference in AE rate leading to dose interruption of 69% with Stivarga in CONCUR study, compared to 35% with fruquintinib. Hence, we view Elunate as a potential next-generation VEGFR inhibitor featuring clinical superiority for CRC in late-line settings.

Figure 43: Fruquintinib showed efficacy advantage (vs Stivarga) in 3L CRC patients

Study	FRESCO		CONCUR				CORRECT	
Patient population (3L CRC)	Mainland China		Chinese patients subgroup (Mainland China, Hong Kong, Taiwan)		All patients (Mainland China, Hong Kong, Taiwan, Vietnam, South Korea)		Global	
Treatment arm	Elunate	Placebo	Stivarga	Placebo	Stivarga	Placebo	Stivarga	Placebo
Patients (n)	278	138	112	60	136	68	505	255
ORR	4.7%	0%	3.6%	0%	4.4%	0%	1.0%	0.4%
DR	62.2%	12.3%	45.5%	6.7%	51.5%	7.4%	41.0%	14.9%
mPFS	3.7 months	1.8 months	2.0 months	1.7 months	3.2 months	1.7 months	1.9 months	1.7 months
mOS	9.3 months	6.6 months	8.4 months	6.2 months	8.8 months	6.3 months	6.4 months	5.0 months

Source: Company data, CMBIS

Figure 44: Fruquintinib showed superior safety (vs Stivarga) in 3L Chinese CRC patients

	ELUNATE® Fruquintinib Capsules		Stivarga® (regorafenib) tablets	
3rd-Line Metastatic Colorectal cancer	FRESCO Study Mainland China [1]		CONCUR Study (Mainland China, HK, Taiwan) [2]	
Treatment arms	ELUNATE®	Placebo	STIVARGA®	Placebo
Patients (n)	278	138	112	60
≥G3 AE (Safety population)	61.1%	19.7%	69.6%	46.7%
SAE (Safety population)	15.5%	5.8%	31.3%	26.7%
VEGFR on-target related AEs:				
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
Off-target (i.e. non-VEGFR) related AEs:				
Hypophosphatemia, ≥G3	0.0%	0.0%	8.0%	0.0%
Hypokalemia, ≥G3	0.7%	0.7%	6.3%	0.0%
Rash/desquamation, ≥G3	0.0%	0.0%	4.4%	0.0%
Lipase increase, ≥G3	0.0%	0.0%	6.3%	1.7%
Hepatic function (Liver function) AEs:				
ALT increased, ≥G3	0.7%	1.5%	7.1%	3.3%
AST increased, ≥G3	0.4%	0.7%	8.9%	0.0%
Blood bilirubin increased, ≥G3	1.4%	1.5%	8.9%	8.3%
Tolerability:				
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%
AE Leading to dose reduction	24.1%	4.4%	23.2%	0.0%
AE Leading to treatment discontinuation	15.1%	5.8%	14.3%	6.7%

Source: Company data, CMBIS

Combination strategy with PD-1mAb to further unleash market potential

Beyond its approved 3L CRC indication in China, fruquintinib is being assessed in two global clinical trials as monotherapy, including i) a global Phase III trial (FRUTIGA, NCT04322539) in 3L CRC, which plans to enroll over 680 patients across 14 countries by 2021E, and ii) a global Phase I trial triple negative breast cancer (TNBC) and HR+/HER- breast cancer.

Underpinned by the increasing market penetration of PD-1 mAb in China, HCM aims to expand fruquintinib's label with PD-1 combinations. The Company is conducting six clinical trials across multiple solid tumors in combination with various PD-1 mAbs (BeiGene's tislelizumab, Genor's geptanolimab and Innovent's sintilimab) in both China and the US, including:

i) A Phase II (NCT03903705) with sintilimab for HCC, endometrial cancer, renal cell carcinoma (RCC) and gastrointestinal cancer (GI) in China. The Company plans to initiate a registrational study in endometrial cancer (EMC) in China by 2H21E. Meanwhile, registration plans for HCC and RCC are under discussion.

ii) A Phase II trial (NCT04179084) for 3L CRC in combination with sintilimab in China.

iii) Two ongoing Phase Ib trials (NCT03977090, NCT03976856) in combination with geptanolimab for CRC and NSCLC respectively in China.

iv) Two Phase Ib clinical trials (NCT04577963, NCT04716634) in combination with tislelizumab for TNBC and multiple solid tumors (including GC, CRC and NSCLC), are ongoing.

Figure 45: Summary of fruquintinib PD-1 mAb combination studies

PD-1	Partner	Indication	Trial location	Status/Expected enrollment
Sintilimab	Innovent	CRC	China	Phase II ongoing
Sintilimab	Innovent	HCC	China	Phase II ongoing
		Endometrial cancer		
		RCC		
		Other GI		
Tislelizumab	BeiGene	TNBC	US	PhaseIb/II ongoing
Tislelizumab	BeiGene	Solid tumors	Korea, China	PhaseIb/II ongoing
Geptanolimab	Genor	CRC	China	Phase Ib ongoing
Geptanolimab	Genor	NSCLC	China	Phase Ib ongoing

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

Meanwhile, the Company is also exploring combination opportunity of fruquintinib with Taxol as 2L treatment for gastric cancer in a Phase III trial (NCT03223376) in China. The primary efficacy endpoint is OS. The Company expects to complete patient enrolment of 700 patients by 2021E.

Competitive landscape of VEGFR inhibitors

The VEGFR-targeted therapeutic space is relatively crowded in China and the US. However, most molecules act on multi-targets (not limited to VEGFR) thus clinical hindered by unwanted toxicity effect. Thanks to its differentiated clinical profile with high kinase

selectivity, we think fruquintinib entails large potential of combination opportunities across multiple indications in early-line settings.

Figure 46: Approved VEGFR-targeted small-molecule inhibitors in the US

Drug	Target	Company	Approval year	Indications
Tivozanib	VEGF-1/2/3, c-kit, PDGR	Aveo Oncology	Mar 2021	r/r RCC
Lenvatinib	VEGFR1/2/3, FGFR 1/2/3/4, PDGFRα, Kit, Ret	Eisai	Feb 2015	Radioactive iodine-refractory DTC, 2L RCC , 1L HCC
Cabozantinib	VEGFR1/2/3, KIT, TRKB, FLT-3, AXL, RET, MET, TIE-2	Exelixis	Nov 2012	RCC, HCC previously treated with sorafenib, MTC
Regorafenib	VEGFR1/2/3, TIE2, PDGFR-β, FGFR, KIT, RET, RAF	Bayer	Sep 2012	CRC previously treated with chemotherapy/anti-VEGF therapy, and, if RAS wild-type, anti-EGFR therapy, GIST following imatinib and sunitinib, 2L HCC
Axitinib	VEGFR 1/2/3, PDGFR, cKIT	Pfizer	Jan 2012	2L RCC
Vandetanib	VEGFR1/2/3, PDGFR, cKIT	Sanofi	Apr 2011	MTC
Pazopanib	VEGFR1/2/3, PDGFR-α/β, c-kit	Novartis	Oct 2009	RCC, 2L soft tissue sarcoma
Sunitinib	VEGFR1/2/3, PDGFR, CSFR, c-KIT	Pfizer	Jan 2006	GIST after disease progression on or intolerance to Imatinib, RCC, pancreatic NET
Sorafenib	RAF1, BRAF, VEGFR 1/2/3, PDGFR, KIT, FLT3, FGFR1, and RET	Bayer	Dec 2005	HCC, RCC, DTC refractory to radioactive iodine treatment

Source: FDA, F&S, CMBIS; Note: HCC: hepatocellular carcinoma; DTC: Differentiated thyroid cancer; MTC: medullary thyroid cancer

Figure 47: Approved VEGFR-targeted small-molecule inhibitors in China

Drug	Target	Company	Approval year	Indications	Estimated monthly cost	NRDL
Donafenib	RET, VEGFR, PDGFR, RAF1	Zelgen Biopharma	Jun 2021	1L HCC	N/A	No
Lenvatinib	VEGFR1/2/3, FGFR 1/2/3/4, PDGFRα, Kit, Ret	Eisai	Sep 2018	1L HCC	US$1,495	Yes
Fruquintinib	**VEGFR1/2/3**	**HCM**	**Sep 2018**	**3L CRC**	**US$1180**	**Yes**
Anlotinib	VEGFR2/3, FGFR 1/2/3/4, PDGFR, c-Kit, Ret	Sino Biopharma	May 2018	SCLC, NSCLC, medullary thyroid carcinoma, soft tissue sarcoma	US$991	Yes
Regorafenib	VEGFR1/2/3, TIE2, PDGFR-β, FGFR, KIT, RET, RAF	Bayer	Mar 2017	2L CRC, GIST previously, HCC previously treated with sorafenib treated with imatinib/sunitinib	US$2,381	Yes
Pazopanib	VEGFR 1/2/3, PDGFR, cKIT	Novartis	Feb 2017	1L RCC	US$2,954s	Yes
Apatinib	VEGFR-2	Hengrui	Oct 2014	3L GC, HCC	US$1,594	Yes

Axitinib	VEGFR 1/2/3, PDGFR, cKIT	Pfizer	Apr 2015	2L RCC	US$1,815	Yes
Sunitinib	VEGFR1/2/3, PDGFR, CSFR, c-KIT	Pfizer	Oct 2007	GIST intolerant to imatinib, RCC, pancreatic NET	US$2,146-2,862	Yes
Sorafenib	RAF1, BRAF, VEGFR 1/2/3, PDGFR, KIT, FLT3, FGFR1, and RET	Bayer	Sep 2006	HCC, RCC	US$1,754	Yes

Source: CDE, F&S, CMBIS; Note: HCC (hepatocellular carcinoma); RCC: renal cell carcinoma; GIST: gastrointestinal stromal tumor; NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer

Figure 48: VEGFR-targeted small-molecule inhibitors under late-stage clinical development in China

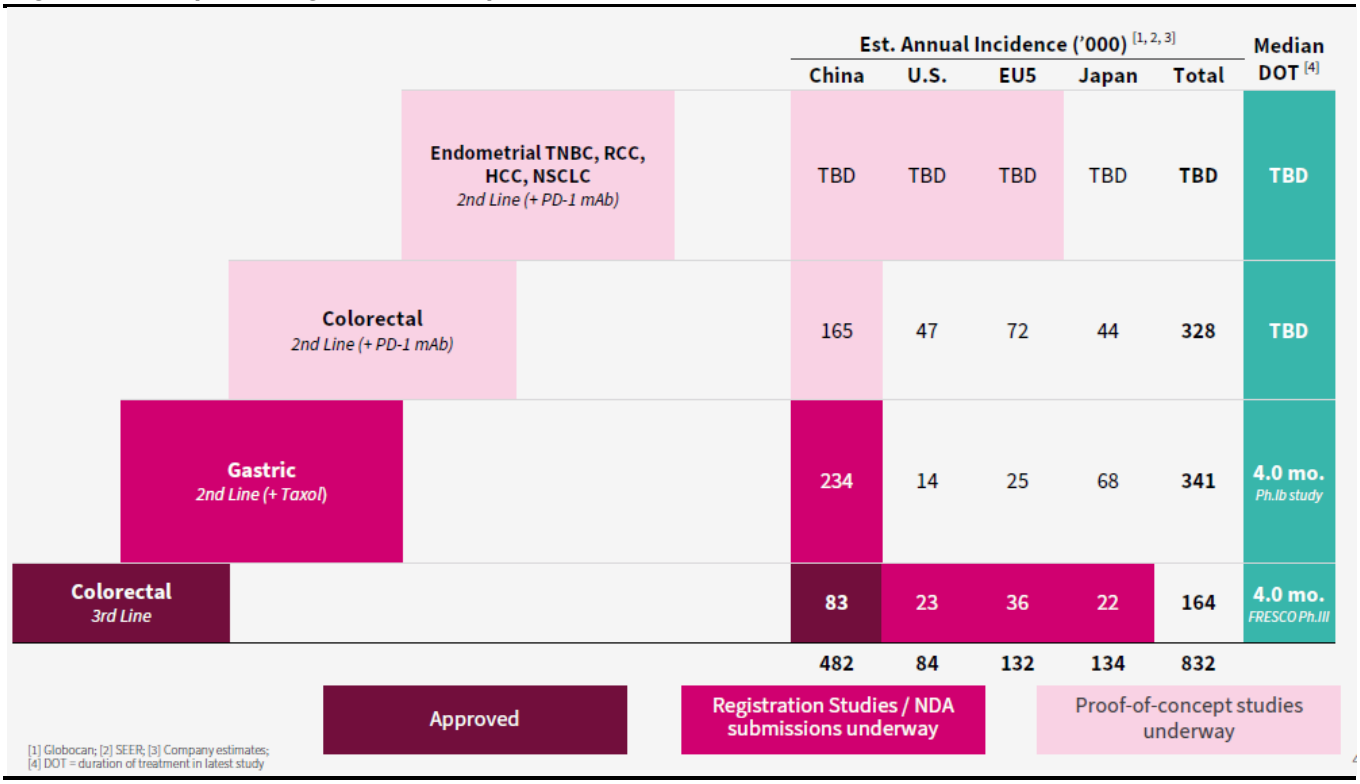
Drug	Target	Company	Indications	Status
Famitinib	VEGFR1/2/3, PDGFR, c-KIT, FLT3	Hengrui	Gastrointestinal stromal tumor	Phase III
			Cervical cancer, NSCLC, urinary system tumors, Intrahepatic cholangiocarcinoma	Phase II
Vorolanib	VEGFR, PDGFR	Betta	Kidney cancer	Phase II
Telatinib	VEGFR2/3, PDGFα, c-Kit	Taizhou Edding	Gastric Cancer	Phase II
Sitravatinib	RET, TYRO3, Axl, MER, VEGFR2, KIT	BeiGene	HCC, gastroesophageal junction Carcinoma	Phase I/II

Source: CDE, F&S, CMBIS; Note: HCC (hepatocellular carcinoma); NSCLC: non-small cell lung cancer

Market opportunity for fruquintinib

As of 2030E, for 3L CRC, we model sales of US$168mn in China, with US$126mn revenue attributable to HCM (assuming HCM to record 75% revenue on China sales). We project subsequent launch of 2L GC in 2024E in China and model risk-adjusted sales of US$257mn in 2L GC with US$193mn revenue attributable to HCM in 2030E. We project risk adjusted sales of US$623mn from fruquintinib in the US/EU/Japan in 2030E, factoring in contribution from 3L CRC indication. We also estimate risk-adjusted sales of US$168mn from fruquintinib's combination with various PD-1 mAbs in China, with US$126mn attributable to HCM in 2030E. Overall, we forecast fruquintinib to record risk-adjusted, attributable global sales of US$1.07bn in 2030E, and risk-adjusted attributable global peak sales of US$1.09bn in 2031E.

Figure 49: Fruquitinnib global market potential



Source: Company data, CMBIS

Figure 50: Fruquintinib revenue build summary

Indication	Targeted patient population	Patients treated with savolitinib	(Expected) year of launch	Probability of success	Risk adjusted sales in 2030E (US$ mn)	% of HCM attributable revenue	HCM attributable revenue in 2030E (US$ mn)
3L CRC (China)	101,049	46,483	2018	-	168	75%	126
2L GC (China)	274,887	104,457	2024	80%	257	75%	193
3L CRC (US)	76,288	5,493	2024	80%	311	-	311
3L CRC (EU/Japan)	76,288	5,493	2024	80%	311	-	311
Various solid tumors combo with PD-1mAb (China)	162,435	45,482	2024/2025	80%	168	75%	126
Total					**1,215**		**1,067**

Source: Company data, CMBIS estimates

HMPL-689, a potentially best-in-class PI3Kδ inhibitor

HMPL-689 is a novel, highly selectively small molecule inhibitor targeting phosphoinositide 3-kinase δ (PI3Kδ) isoform. It is designed to potentially become a BIC PI3Kδ inhibitor with improved pharmacokinetic profile and superior PI3Kδ isoform selectivity sparing PI3Kα and PI3Kγ. Thanks to its highly differentiated clinical profile, it allows reduced daily dosage and enables longer treatment duration vs first-generation PI3K inhibitors which are commonly hampered by hepatotoxicity. HCM owns global rights.

Figure 51: Clinical development plan of HMPL-689

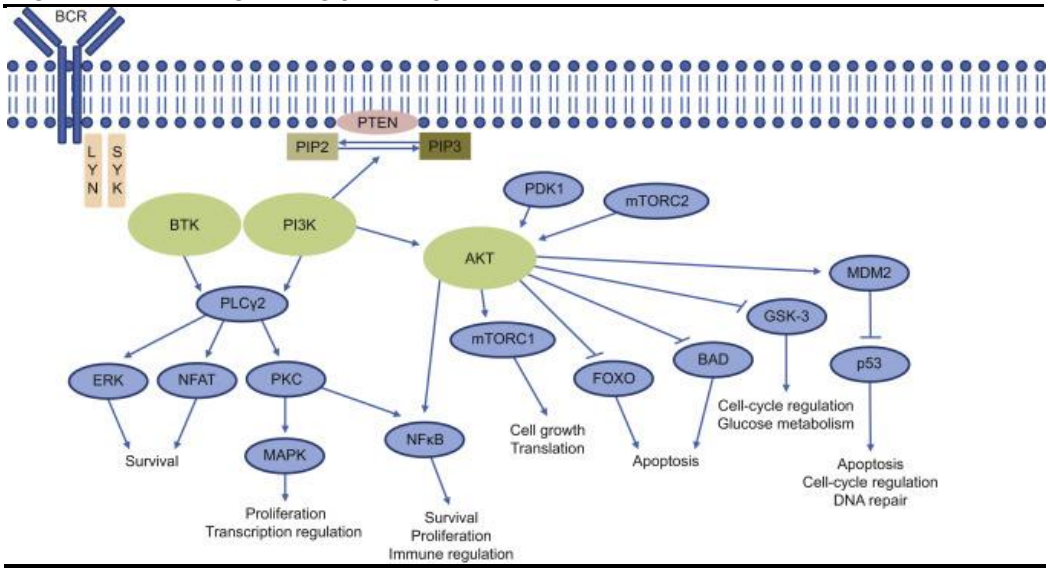
Indication	Type of treatment	China status	Global status	Upcoming event
2L MZL/3L FL	Mono	Phase II registration intent	-	Expected to complete patient enrollment in 2H22E
Indolent NHL	Mono	Phase Ib	-	Phase Ib dose expansion study ongoing in 3L CLL/SLL, MCL, DLBCL, and T-cell lymphoma
Indolent NHL	Mono	-	US/EU: Phase Ib	To engage with regulatory authorities to discuss potential registration pathway in 2H21E

Source: Company data, CMBIS

Mechanism of action of HMPL-689

PI3Ks are involved in the regulation of many signaling pathways, which play key roles in cell proliferation, growth, survival, and metabolism. Over-activation of PI3K pathway has been observed to be a hallmark in B-cell malignancies (Philips T et al, 2020). PI3Kδ is the main isozyme responsible for the activation of the PI3K pathway in B-cell signaling. PI3Kδ inhibitors (vs other PI3K isoforms) offer the advantage of avoiding side effects, such as disruption of insulin signaling (PI3Kα) and spermatogenesis (PI3Kβ) (Shin N et al 2020).

Figure 52: PI3K signalling pathway



Source: Philips T et al, 2020, CMBIS

Enhanced PK profile and high selectivity among PI3K class

Designed with enhanced pharmacokinetic (PK) profile, HMPL-689 showed higher potency (achieving inhibitory activity at much lower IC50 Level) and greater selectivity to PI3Kδ isoform, compared to competing PI3K inhibitors in pre-clinical study.

Figure 53: HMPL-689 showed greater potency and selectivity vs other PI3K inhibitors in pre-clinical study

Enzyme IC50 (nM)	HMPL-689	ZYDELIG (idelalisib)	COPIKTRA (duvelisib)	ALIQOPA (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)
PI3Kδ human whole blood CD63+	3	14	15	N/A
PI3Kβ (fold vs. PI3Kδ)	87 (109x)	293 (147x)	8 (8x)	3.7 (5x)

Source: Company data, CMBIS

HMPL-689 showed promising clinical activity in FL/MZL

HCM has commenced a multi-center, single-arm, open-label, registration-intent Phase II trial (NCT04849351) of HMPL-689 as monotherapy for 2L+marginal zone lymphoma (MZL) and 3L+ follicular lymphoma (FL) patients in China since Apr 2021. The trial plans to enroll 100 FL patients and 80 MZL patients, respectively. The primary point is ORR. The dosing regimen is set to be 30 mg HMPL-689 oral monotherapy once per day in 28-day treatment cycles. The Company expects to complete patient enrollment for FL and MZL by 1H22E/2H22E, respectively.

The initiation of the Phase II trial is based on promising preliminary results of Phase Ib expansion study in China, showing HMPL-689's favorable tolerability and manageable toxicity profile. According to Phase I intention to treat (ITT) study data (n=56) presented at American Society of Hematology (cut-off date Sep 2020), ORR was 48.2% and CR rate was 10.7%. On safety, HMPL-689 was well tolerated at recommended Phase II dose (RP2D) and its overall safety profile looks numerically favorable compared to other PI3K peers.

Figure 54: HMPL-689 demonstrated promising clinical activity in Phase I dose escalation study

Study	A Phase I dose escalation study (NCT03128164) in Chinese patients with relapsed/refractory lymphoma (cut-off date: Sep 2020)
Patient enrolled	56
Indication	CLL/SLL: 5 (8.9%); FL: 23 (41.1%); MZL: 7 (12.5%); DLBCL: 9 (16.1%); MCL: 9 (16.1%); HL: 3 (5.4%)
Prior Systemic therapies (median)	2
≥ 3 prior systemic therapy	26 (46.4%)
Efficacy	
ORR	48%
CR	11%
PR	37%
SD	34%

Time on treatment	5.6 months
Time to response	1.8 months
Duration of response	9.2 months
PFS	10.1 months
1-year PFS rate	40%

Source: Company data, CMBIS

Figure 55: HMPL-689 showed encouraging safety profile (All AEs / Grade ≥ 3 AEs)

Drug	HMPL-689	Zydelig (idelalisib)	Aliqopa (copanlisib)	Copiktra (duvelisib)	Ukoniq (umbralisib)	Parsaclisib	Parsaclisib	Zandelisib	Zandelisib
Study	**Phase I dose escalation study**	Pooled trial analysis	Phase II pivotal trial	Pooled trial analysis	Pooled trial analysis	Phase I dose escalation study	Phase II trial (CITADEL-204)	Phase I intermittent dosing	Phase I dose escalation study
n	**56**	146	168	442	221	72	100	21	30
Neutropenia	**43%/11%**	53%/25%	32%/25%	34%/30%	33%/16%	44%/20%	13%/9%	N/A/14%	45%/13%
Anemia	**16%/0%**	28%/2%	N/A	20%/11%	27%/3%	31%/8%	14%/5%	N/A/0%	13%/0%
Thrombocytopenia	**11%/0%**	26%/6%	22%/8%	17%/10%	26%/4%	35%/10%	N/A	N/A/0%	22%/0%
Diarrhea or colitis	**<5%/<5%**	47%/14%	36%/5%	50%/23%	58%/10%	36%/ 9%	44%/11%	N/A/4%	45%/19%
Rash	**11%/5%**	21%/3%	15%/2%	31%/9%	18%/3%	31%/6%	17%/2%	N/A/2%	42%/13%
ALT increased	**27%/2%**	50%/19%	N/A	40%/8%	33%/8%	28%/1%	26%/4%	N/A/0%	39%/6%
AST increased	**21%/2%**	41%/12%	N/A	37%/6%	32%/7%	29%/1%	19%/2%	N/A/0%	25%/6%
Pyrexia	**14%/0%**	28%/2%	N/A	26%/2%	N/A	18%/1%	13%/s1%	N/A	N/A
Pneumonia	**25%/16%**	25%/16%	21%/14%	21%/15%	PJP prophylaxis recommended	N/A	7% with PJP prophylaxis	PJP prophylaxis	N/A
Hypertension	**7%/5%**	N/A	35%/27%	N/A	N/A	7%/0%	N/A	N/A	N/A
Hyperglycemia	**11%/2%**	N/A	54%/39%	N/A	N/A	10%/1%	N/A	N/A	N/A

Source: FDA, Company data, CMBIS

Globally, a multi-center, open-label, two-stage Phase Ib study (NCT03786926) is being conducted in the US/UK for patients with indolent NHL (including CLL, SLL, FL, MZL, LPL/WM and MCL). The Company plans to engage with regulatory authorities to discuss potential registration pathway in 2H21E.

Competitive landscape of PI3K inhibitors

In the US, there are five PI3K inhibitors, namely, idelalisib, copanlisib, duvelisib, alpelisib and umbralisib, approved by the US FDA. In 2020, aggregated global sales of four approved PI3K inhibitors (idelalisib, copanlisib, duvelisib, alpelisib) were US$462mn, while sales of three approved PI3K inhibitors indicated for hematological malignancy were US$142mn, according to Evaluate Pharma.

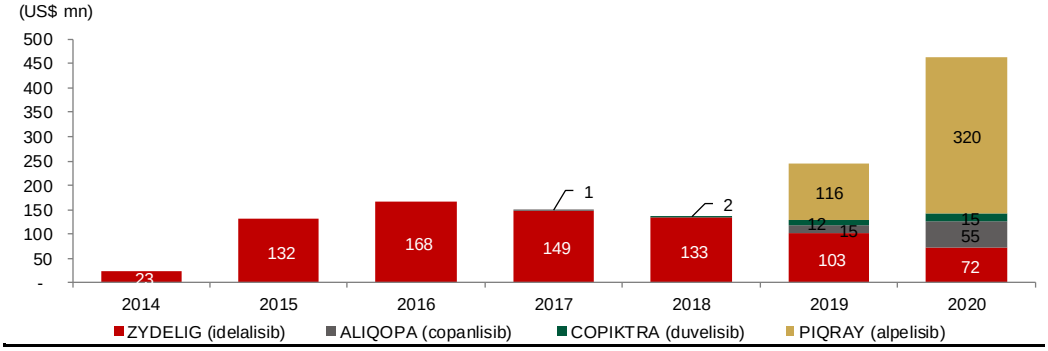
Figure 56: FDA approved PI3K inhibitors in the US

Drug	Target	Company	Approval year	Approved indications	Administration
ZYDELIG (idelalisib)	PI3Kδ	Gilead	2014	r/r CLL in combination with rituximab r/r FL with at least two prior systemic therapies r/r SLL with at least two prior systemic therapies	Oral
ALIQOPA (copanlisib)	pan-PI3K	Bayer	2017	r/r FL with at least two prior systemic therapies	I.V.

COPIKTRA (duvelisib)	PI3Kδ, PI3Kγ	Takeda/ Verastem/ Secura Bio	2018	r/r CLL/SLL with at least two prior systemic therapies r/r FL with at least two prior systemic therapies	Oral
PIQRAY (alpelisib)	PI3Kα (PIK3CA)	Novartis	2019	HR+/HER2-, PIK3CAm+ breast cancer	Oral
UKONIQ (umbralisib)	PI3Kδ	TG Therapeutics	2021	r/r MZL with at least one prior anti-CD20-based regimen r/r FL with at least three prior lines of systemic therapy	Oral

Source: FDA, CMBIS; Notes: FL: follicular lymphoma; CLL/SLL: Chronic lymphocytic leukemia/small lymphocytic lymphoma; BC: breast cancer

Figure 57: Global sales of FDA approved PI3K inhibitors



Source: Evaluate Pharma, CMBIS

In China, none of PI3K inhibitors have been approved, while more than 20 PI3K drug candidates have entered intos clinical development. We think the market landscape for PI3K inhibitors is crowded given that three molecules have filed NDA and four are in pivotal trials. However, HMPL-689 has unique edge given its differentiated clinical profile.

Figure 58: Late-stage PI3K inhibitor candidates under development in China

Compound	Target	Company	Progress	Indications
Copanlisib	PI3Kδ/PI3Kα	Bayer	NDA	FL
Duvelisib	PI3Kγ/PI3Kδ	CSPC	NDA	FL
YY-20394	PI3Kδ	YL-Pharma, Hengrui	NDA	FL
Alpelisib	PI3Kα	Novartis	Phase III	BC, TNBC
Buparlisib	Pan-PI3K	Adlai Nortye, Novartis	Phase III	HNSCC
Taselisib	PI3Kα	Roche	Phase III	BC
Inavolisib	PI3Kα	Roche	Phase III	BC
Parsaclisib	PI3Kδ	Innovent	Pivotal Phase II	FL, MZL
HMPL-689	**PI3Kδ**	**HCM**	**Phase I/ Phase II (registration intent)**	**FL/MZL, indolent NHL**
BEBT-908	PI3K	BeBetter Med	Phase II	CLL/SLL, FL, MZL, DLBCL, PTCL
TQB3525	PI3Kγ/PI3Kδ	Sino Biopharm	Phase II	FL, MCL
SHC014748M	PI3Kδ	SanHome	Phase II	PTCL, FL, MZL

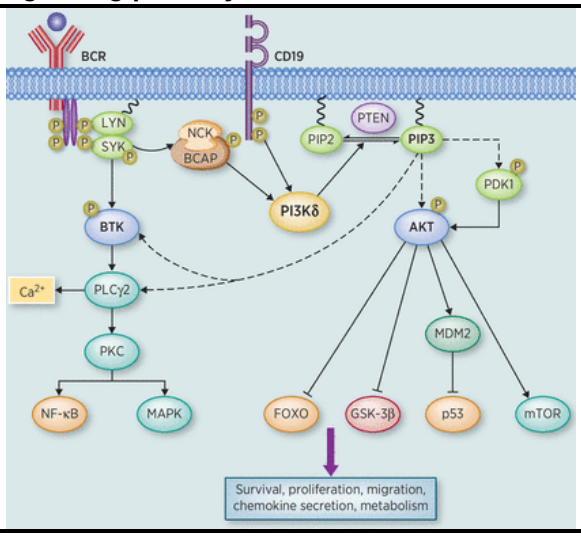
Source: Insight, company data, CMBIS; Note: FL: follicular lymphoma; CLL/SLL: Chronic lymphocytic leukemia/small lymphocytic lymphoma; BC: breast cancer; PTCL: peripheral T-cell lymphoma; DLBCL: diffuse large B-cell lymphoma; MZL: marginal zone lymphoma; HNSCC: head and neck squamous cell carcinomas

Next-wave of innovation

HMPL-523, a highly selective Syk inhibitor

HMPL-523 is a highly selective, oral, small molecule inhibitor of spleen tyrosine kinase (Syk), a key upstream kinase to PI3K and BTK involved in B-cell signaling pathway, as a potential therapy for autoimmune diseases and oncology. HCM owns global rights.

Figure 59: Syk signalling pathway



Source: Yang Q et al, 2015, CMBIS

Some biotech companies have experienced a bumpy road in the development of Syk inhibitors, exemplified by fostamatinib's Phase III trial failure for rheumatoid arthritis (RA). Developed by AstraZeneca/Rigel, fostamatinib was investigated in combination with methotrexate in patients with inadequate response to TNF-α inhibitor. Although efficacy was proven statistically significant in one of the treatment regimens (100 mg BID for 24 weeks), overall response rate was low. Its safety and tolerability profile (in particular high blood pressure as a result of off-target kinase activity) was also found to limit its potential clinical use. However, HMPL-523 was designed to have high tissue distribution, and was found to be well tolerated in pre-clinical study.

Figure 60: Clinical development plan of HMPL-523

Indication	Type of treatment	China status	Global status	Upcoming event
2L ITP	Mono	Phase I/Ib	-	Completed. To initiate Phase III trial in 2H21E
Multiple sub-types of B-cell malignancies	Mono	Phase Ib	-	Enrollment completed
Indolent NHL	Mono	-	US/EU: Phase Ib; Australia: Phase Ib	-
AIHA	Mono	Phase II		In planning

Source: Company data, CMBIS; Note: ITP: immune thrombocytopenia purpura; AIHA: autoimmune hemolytic anemia

Immune thrombocytopenia purpura (ITP): A randomized, double-blinded, placebo-controlled Phase Ib trial (NCT03951623) is being investigated to evaluate the safety and

preliminary efficacy of HMPL-523 for 2L or above ITP treatment, with a plan to enroll 50 to 60 patients in China. Dose escalation is near completion which supports initiation of a Phase III trial in 2H21E.

Indolent NHL: Two Phase I/Ib studies (NCT02503033/NCT02857998) in China and Australia, respectively, is ongoing for patients with indolent NHL and multiple subtypes of B-cell malignancies with over 200 patients enrolled. In addition, HCM has initiated a Phase Ib study (NCT03779113) in indolent NHL in the US/EU.

Autoimmune hemolytic anemia (AIHA): Following the encouraging data seen in Phase Ib study in the autoimmune disorder ITP, HCM intends to initiate a Phase II study in patients with AIHA, another autoimmune disorder.

Competitive landscape of Syk inhibitors

Globally, Rigel's Tavalisse (fostamatinib) is the only FDA approved oral Syk inhibitor, indicated for ITP patients with insufficient response to previous treatment. We think the market landscape in Syk-targeted therapeutic space is relatively favorable with a hand of molecules under mid-to-late stage clinical development, focusing on autoimmune disease such as rheumatoid arthritis (RA), warm autoimmune hemolytic anemia, as well as hematological cancers.

Figure 61: Syk inhibitors under clinical development in the US

Drug	Target	Company	Status	Indications
Fostamatinib	SYK	Rigel	Phase III	COVID-19, warm autoimmune hemolytic anemia
Entospletinib	SYK	Kronos Bio	Phase III	FLT3-mutated AML
SKI-O-703	SYK	Oscotec	Phase II	ITP, RA
Gusacitinib	JAK, SYK	Asana BioSciences	Phase II	Chronic eczema
Cerdulatinib	SYK, JAK1, JAK3, TYK2	Dermavant	Phase I/II	Vitiligo (白癜風), Atopic dermatitis
HMPL-523	**SYK**	**HCM**	**Phase Ib**	**indolent NHL**

Source: Insight, NextPharma, various company data, CMBIS; Note: RA: rheumatoid arthritis; NHL: non-Hodgkin lymphoma; AML: acute myeloid leukemia

In China, none of SYK inhibitors have been approved. There are only three SYK-targeted therapies currently under clinical investigation, including HCM's HMPL-523, Sino Biopharm's TQB3473 and CSPC's SYHX1901.

Figure 62: Syk inhibitors under clinical development in China

Drug	Target	Company	Status	Indications
HMPL-523	**SYK**	**HCM**	**Phase I/II**	**2L ITP, multiple sub-types of B-cell malignancies, AIHA**
TQB3473	SYK	Sino Biopharm	Phase I	Hematological malignancies
SYHX1901	JAK/SYK	CSPC	Phase I	SLE

Source: Insight, NextPharma, CMBIS; Note: SLE: systemic lupus erythematosus

HMPL-453, a potent pan-FGFR1/2/3 small molecule inhibitor

HMPL-453 is a highly selective, small molecule targeting fibroblast growth factor receptor (FGFR) 1/2/3. FGFR is validated therapeutic target. Aberration of FGFR is associated with tumor growth and promotion of angiogenesis. In pre-clinical evidence, HMPL-453 exhibited strong potency with IC50 in low nanomolar range. Its good selectivity was revealed in the screening against 292 kinases. HMPL-453 exhibited strong anti-tumor activity that correlated with target inhibition in tumor models with abnormal FGFR activation.

Moreover, it showed good pharmacokinetic profile characterized by rapid absorption, good bioavailability, moderate tissue distribution and moderate clearance in all pre-clinical animal species. On safety, HMPL-453 was found to have a low likelihood of drug-to-drug interaction. HCM owns global rights in HMPL-453.

A Phase II trial (NCT04353375) of HMPL-453 is ongoing in China, evaluating HMPL-453 as a 2L+ treatment for advanced intrahepatic cholangiocarcinoma (IHCC). IHCC a type of cancer that develops in bile ducts with annual incidence of 116,500 cases in China. FGFR alternation, most commonly FGFR2 fusion, is found in 20% of IHCC patients (Cleary J et al, 2020).

Figure 63: Multiple oncologic genetic alternations are found in FGFR pathway

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

Source: Company data, CMBIS

Competitive landscape of pan-FGFR inhibitors

Globally, there are three US FDA approved pan-FGFR inhibitors, namely Balversa (erdafitinib), Pemazyre (pemigatinib) and Truseltiq (infigratinib). According to Incyte, Pemazyre raked in US$31.4mn sales in 1H21.

Developed by Incyte, pemigatinib was approved by the US FDA in Apr 2020, for the treatment of previously treated locally advanced/metastatic cholangiocarcinoma with FGFR2 fusion or other rearrangement. The approval was based on the results from a single-arm Phase II study (FIGHT-202, NCT02924376) in 107 2L cholangiocarcinoma patients. The ORR was 36%, including 3 patients (3%) with CR and 35 patients (33%) with PR. The median DoR was 7.5 months, and median PFS was 6.9 months.

Figure 64: US FDA approved FGFR targeted therapies

Drug	Target/modality	Company	Approval year	Indications
Balversa (Erdafitinib)	FGFR1/2/3/4 small molecule inhibitor	J&J	Apr 2019	2L Urothelial cancer
Pemazyre (Pemigatinib)	FGFR1/2/3 small molecule inhibitor	Incyte	Apr 2020	2L Cholangiocarcinoma
Truseltiq (Infigratinib)	FGFR1/2/3 small molecule inhibitor	QED Therapeutics	May 2021	2L Cholangiocarcinoma

Source: Company data, FDA, CMBIS

Figure 65: Selective FGFR-targeted therapies under late-stage clinical development globally

Drug	Target	Modality	Company	Status	Indications
Futinatinib	FGFR1/2/3/4	Small molecule inhibitor	Taiho Oncology	Phase III Phase II	Cholangiocarcinoma HCC, UC, GC.GEJ, breast cancer
Infigratinib	FGFR1/2/3	Small molecule inhibitor	QED Therapeutics	Phase III	UC
Derazantinib	FGFR1/2/3	Small molecule inhibitor	Basilea/Sinovant	Phase II	Cholangiocarcinoma
Bemarituzumab	FGFR2	Small molecule inhibitor	Five Prime Therapeutics	Phase II	Gastric Cancer
Debio1347	FGFR1/2/3	Small molecule inhibitor	Debiopharm	Phase II	Solid tumors
E-7090	FGFR1/2/3	Small molecule inhibitor	Eisai	Phase II	Cholangiocarcinoma

Source: Company data, NextPharma, CMBIS; Note: HCC: hepatocellular carcinoma; UC: urothelial Cancer; GC/GEJ: gastric cancer or gastroesophageal cancer

Although none of FGFR-targeted therapies have been approved in China, the competitive landscape in FGFR space is crowded, given Innovent's Pemigatinib has filed NDA to NMPA and two other molecules have advanced to Phase III trials.

Figure 66: Selective FGFR-targeted therapies under late-stage clinical development in China

Drug	Target	Modality	Company	Status	Indications
Pemigatinib	FGFR1/2/3	Small molecule inhibitor	Innovent	NDA filed	Cholangiocarcinoma
Erdafitinib	Pan-FGFR	Small molecule inhibitor	Xian Janssen	Phase III Phase IIa	UC Cholangiocarcinoma, GC/GEJ
Infigratinib	FGFR1/2/3	Small molecule inhibitor	LianBio	Phase III Phase IIa	Cholangiocarcinoma GC/GEJ
HMPL-453	**FGFR1/2/3**	**Small molecule inhibitor**	**HCM**	**Phase II**	**Cholangiocarcinoma**
Bemarituzumab	FGFR2	mAb	Zai Lab	Phase II	GC/GEJ

Derazantinib	FGFR 1/2/3/4	Small molecule	Sinovant/ Basilea Pharma	Phase II	Cholangiocarcinoma
Roblitinib (FGF401)	FGFR4	Small molecule inhibitor	Everest Medicines	Phase II	HCC
Fisogatinib	FGFR4	Small molecule inhibitor	CStone	Phase II	HCC
ICP-192	Pan-FGFR	Small molecule inhibitor	Innocare	Phase II	Cholangiocarcinoma, UC
ABSK-091	Pan-FGFR	Small molecule inhibitor	Abbisko	Phase I/II	Various solid tumors (UC, cholangiocarcinoma, gastric cancer, endometrial cancer and lung cancer.

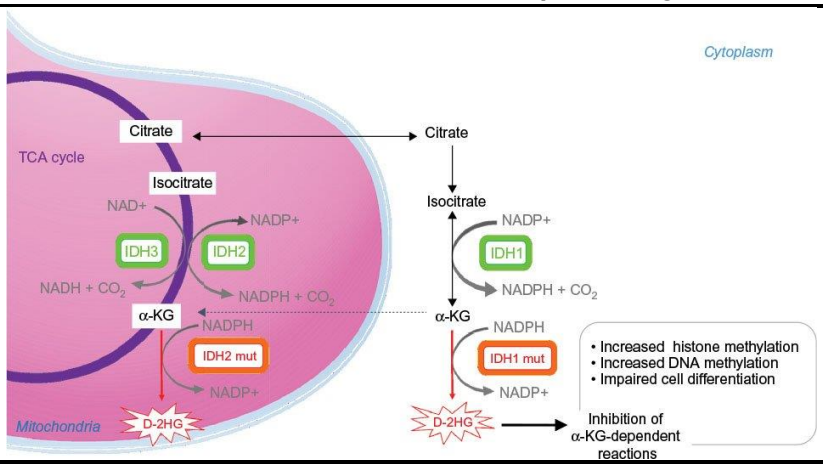
Source: Company data, Pharmcube, CMBIS; Note: HCC: hepatocellular carcinoma; UC: urothelial Cancer; GC/GEJ: gastric cancer or gastroesophageal cancer

HMPL-306, a dual-targeting IDH1/IDH2 inhibitor

HMPL-306 is a potent small molecule dual-inhibitor of isocitrate dehydrogenase 1 and 2 (IDH1/IDH2) enzymes. IDH1 and IDH2 mutations been implicated in various solid and haematological malignancies including gliomas/secondary glioblastomas (80%), bone sarcoma (60%), intrahepatic cholangiocarcinoma (20%) and acute myeloid leukaemia (10%). Both targets have been validated given the approval of two IDH1 or IDH2-targeted therapies globally, namely ivosidenib (IDH1 inhibitor) and enasidenib (IDH2 inhibitor).

Mutant IDH1 and IDH2 have been known to switch to the other form when targeted by either inhibitor of mutant IDH1 or IDH2 alone. By targeting both IDH1 and IDH2 mutations, HMPL-306 could potentially provide therapeutic benefits in cancer patients harbouring either IDH mutation and address acquired resistance to IDH inhibition through isoform switching. Moreover, HMPL-306 was found to demonstrate comparable efficacy in preclinical model with wide safety window. Designed with higher penetration of blood-brain barrier, HMPL- 306 entails therapeutic potential for gliomas.

Figure 67: IDH1 and IDH2 mutations as novel therapeutic targets



Source: Mondesir et all, 2016, CMBIS

Figure 68: IDH1/2 mutations are frequent genetic alterations in AML, glioma & solid tumors

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

Source: Company data, CMBIS

Clinical development plan of HMPL-306

In China, HMPL-306 is being evaluated in a Phase I trial (NCT04272957) as monotherapy in patients with relapsed or refractory hematological malignancies with IDH1 and/or IDH2 mutation. Dose escalation may complete in late 2021E or early 2022E.

HCM recently initiated a US/EU based Phase I trial (NCT04762602) to evaluate HMPL-306 as monotherapy in patients with solid tumors. Moreover, a US Phase I trial (NCT04764474) has been initiated in patients with IDHm+ hematological malignancies with the first patient dosed in May 2021.

Competitive landscape

To date, US FDA has approved one IDH1 inhibitor and one IDH2 inhibitor, namely Ivosidenib and Enasidenib, respectively. None of IDH/IDH2 dual-targeting therapy has been approved yet. The market landscape looks relatively favorable with only a handful of drugs candidates under clinical development in both China and the US. Ivosidenib garnered US$121.1mn sales in 2020, according to Agios.

Figure 69: Approved IDH1 or IDH2-targeted therapies in the US

Drug	Target	Company	Year of first US FDA approval	Indications
Tibsovo (Ivosidenib)	IDH1	Servier, Celgene (BMS), Agios	Jul 2018	IDH1m+ AML, 1DH1m+ cholangiocarcinoma
Idhifa (Enasidenib)	IDH2	Servier, Celgene (BMS), Agios	Aug 2017	r/r AML with IDH2 mutation

Source: Company data, FDA, CMBIS; Note: AML: acute myeloid leukemia

Figure 70: IDH1/ IDH2-targeted therapies under clinical development in the US

Drug	Target	Company	Status	Indications
AG-881 (Vorasidenib)	IDH1/2	Agios/Servier	Phase III	Glioma, AML
Mobocertinib	IDH1	Daiichi Sankyo	Phase II	Glioma
IDH305	IDH1	Novartis	Phase II	Glioma, AML
FT-2102 (Olutasidenib)	IDH1	Forma	Phase I/II	AML, MDS, Glioma

Source: Company data, pharmacube, CMBIS; Note: AML: acute myeloid leukemia

Figure 71: IDH1/IDH2-targeted therapies under clinical development in China

Drug	Target	Company	Status	Indications
Tibsovo (Ivosidenib)	IDH1	Agios, Servier, Cstone	NDA accepted	r/r AML with IDH1 mutation
Enasidenib	IDH1/2	Celgene/BMS	Phase III	Advanced Acute AML
TQB3455	IDH2	Sino Biopharm	Phase I	Solid tumor, AML
TQB3454	IDH1	Sino Biopharm	Phase I	Hematologic malignancies
SH1573	IDH2	Sanhome	Phase I	AML
KY100001	IDH1	KPC Pharma	Phase I	Solid tumor
HMPL-306	**IDH1, IDH2**	**HCM**	**Phase I**	**Solid tumor, hematologic malignancies**

Source: Company data, pharmacube, CMBIS; Note: AML: acute myeloid leukemia

Tazemetostat, EZH2 inhibitor in-licensed from Epizyme

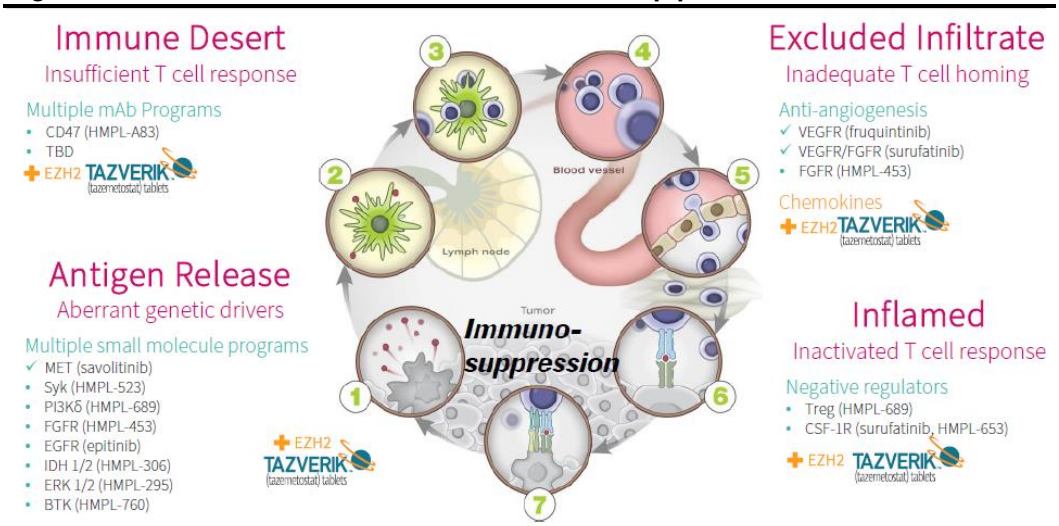
In Aug 2021, HCM entered into collaboration with Epizyme to develop, manufacture and commercialize TAZVERIK (Tazemetostat) in Greater China. HCM is entitled to pay US$25mn upfront payment, US$285mn potential regulatory and commercial milestones, and tiered royalties of mid-teen to low twenties percentage.

Originally developed by Epizyme, tazemetostat is a first-in-class EZH2 small molecule inhibitor, approved by the US FDA under accelerated approval, for the treatment of i) patients with epithelioid sarcoma (ES) not eligible for compete resection, and ii) patients with relapsed/refractory EZH2+ follicular lymphoma (EZH2+ r/r FL) who have received at least two prior systemic therapies and r/r FL patients without satisfactory alternative treatment options.

Unique MoA bringing in synergies across internal pipeline

Tazemetostat inhibits EZH2 which allows transcriptions of genes involved in functions such as cell cycle control, and thereby inhibiting cell proliferation. Thanks to its epigenetic regulating mechanism and favourable safety profile, Tazemetostat features synergistic potential with HCM internal pipeline across various indications in hematological malignancies and solid tumors.

Figure 72: Tazemetostat fits well into HCM's broad pipeline



Source: Company data, CMBIS

The US FDA's approval in ES was based on an open-label, single-arm Phase II trial (EZH-202 cohort 5 study, NCT02601950). In the total 62 patients, the ORR was 15%, with 1.6% achieving CR and 13% achieving PR. Among all responders, 67% had DoR of six months or longer. Serious adverse reactions occurred in 37% of patients, but overall tazemetostat is well tolerated.

The approval in FL was based on an open-label, single-arm, multi-center Phase II trial (Study E7438-G000-101, NCT01897571). Among the 42 EZH2M+ 3L FL patients treated with tazemetostat, the ORR was 69%, with 12% achieving CR and 57% achieving PR. Among responders, 67% had DoR of six months or longer. Serious adverse reactions occurred in 37% of patients. The median DOR was 10.9 months and ongoing. Among the 53 WT EZH2 3L FL patients treated, the ORR was 34%, with 4% of patients achieving CR and 30% achieving PR. The medium DoR was 13 months. Serious adverse reactions occurred in 30% of patients. Eight patients (8%) discontinued due to adverse reaction, with no reported deaths or black box warnings.

Figure 73: Efficacy results of Tazemetostat's pivotal trials for ES, EZH2+FL, and WT FL

Follicular Lymphoma

	EZH2 Mutant N=42	EZH2 Wild-Type N=53
Overall Response Rate (95% CI)*	69% (53%, 82%)	34% (22%, 48%)
Complete Response	12%	4%
Partial Response	57%	30%
Duration of Response (in months)		
Median (95% CI)	10.9 (7.2, NE)	13.0 (5.6, NE)
Range	0.0+, 22.1+	1, 22.5+

Epithelioid Sarcoma

	N=42
Overall Response Rate (95% CI)*	15% (7%, 26%)
Complete Response	1.6%
Partial Response	13%
Duration of Response	
% with duration ≥ 6 months	67%
Range in months	3.7, 24.5+

Source: Company data, CMBIS

Figure 74: Safety data of Tazemetostat's pivotal trials for ES, EZH2+FL, and WT FL

Patients with r/r/ Follicular Lymphoma (AEs ≥10%)

N=99	All Grades	Grade 3 or 4
General		
Fatigue[a]	36%	5%
Pyrexia	10%	0%
Infections		
Upper respiratory tract infection[b]	30%	0%
Lower respiratory tract infection[c]	17%	0%
Urinary tract infection[d]	11%	2%
Gastrointestinal		
Nausea	24%	1%
Abdominal pain[e]	20%	3%
Diarrhea	18%	0%
Vomiting	12%	1%
Musculoskeletal and connective tissue		
Musculoskeletal pain[f]	22%	1%
Skin and subcutaneous tissue		
Alopecia	17%	0%
Rash[g]	15%	0%
Respiratory and mediastinal system		
Cough[h]		
Nervous system		
Headache[i]	13%	0%

Patients with Epithelioid Sarcoma (AEs ≥10%)

N=62	All Grades	Grade 3 or 4
General		
Pain[a]	52%	7%
Fatigue[b]	47%	2%
Gastrointestinal		
Nausea	36%	0%
Vomiting	24%	0%
Constipation	21%	0%
Diarrhea	16%	0%
Abdominal pain[c]	13%	2%
Metabolism and nutrition		
Decreased appetite	26%	5%
Respiratory, thoracic & mediastinal		
Cough	18%	0%
Dyspnea[d]	16%	5%
Vascular		
Hemorrhage[e]	18%	5%
Nervous system		
Headache	18%	0%
Investigations		
Weight decreased	16%	7%

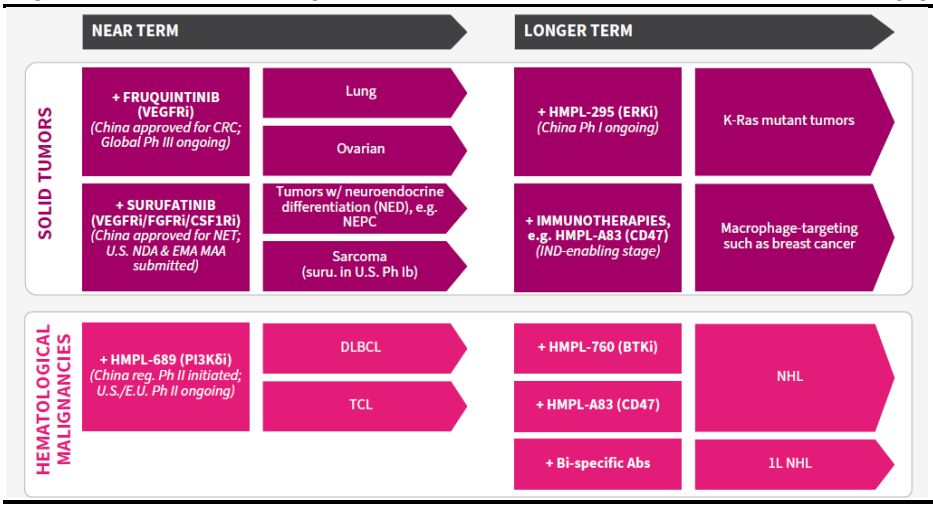
Source: Company data, CMBIS

Clinical development plan of tazemetostat

In China, HCM plans to seek approval for tazemetostat in various haematological and solid tumors, including ES, FL and diffuse large b-cell lymphoma (DLBCL). We expect synergistic combination opportunities of tazmemtostat with HMPL-689 in DLBCL and cutaneous T-cell lymphoma (CTL). For solid tumors,s the Company plans to explore combination potential with fruquintinib in lung cancer and ovarian cancer, as well as with surufatinib in tumors with endocrine differentiation (NED) and sarcoma.

HCM plans to participate in Epizyme's ongoing global registrational study (EZH-302) of tazemetostat in combination with rituximab + lenalidomide (R^2) in 2L FL. With IND filing approved by NMPA in Jul 2021, the Company expects a bridging study of 30-40 patients for NDA submission, while subject to CDE approval. EZH-302 (NCT04224493) study is randomized, double-blinded, active controlled global Phase Ib/III confirmatory trial assessing tazemetostat in combination with rituximab and lenalidomide (R^2), compared with R^2 plus placebo, followed by maintenance tazemetostat or placebo in 2L+FL. The trial is expected to enroll approximately 500 FL patients.

Figure 75: Combination potential of Tazemetostat with HCM's internal pipeline



Source: Company data, CMBIS

Competitive landscape and market opportunity

Competition among the EZH-targeted therapeutic field is mild, with tazemetostat being the only US FDA approved EZH2 inhibitor. Tazemetostat recorded US$11.5mn/US$14.2mn US sales in 2020/1H21, respectively, according to Epizyme. We view further China sales growth trajectory of tazemetostat heavily hinges on combination strategies within HCM's internal pipeline.

Figure 76: Selective EZH targeted therapies under clinical development in China

Drug	Target	Company	Status	Indications
Tazemetostat	**EZH2**	**Epizyme, HCM**	**To commence China arm of global Phase III study**	**2L FL**
SHR2554	EZH2	Hengrui	Phase I/II	Castration resistant prostate cancer
HH2853	PRC2/ EZH1/2	Haihe Pharma	Phase I	Hematological and solid tumors
XNW5004	EZH2	Sinovent	Phase I	Hematological and solid tumors

Source: Company data, insight, CMBIS

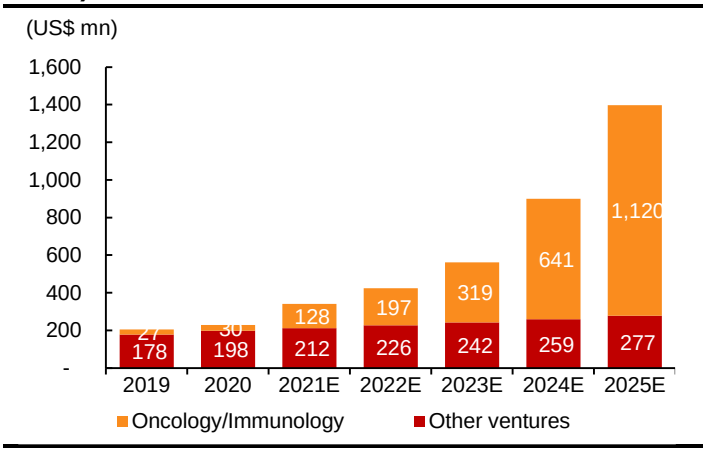
Financial analysis

Expecting breakeven in 2025E

The Company generated US$205mn, US$228mn and US$157mn in 2019/ 2020/ 1H21, primarily driven by i) revenue from other ventures, ii) sales and royalty revenue from Elunate in China, and iii) licensing and research fees charged in connection with out-licensing molecules/ providing research development services via the Oncology/ Immunology operation.

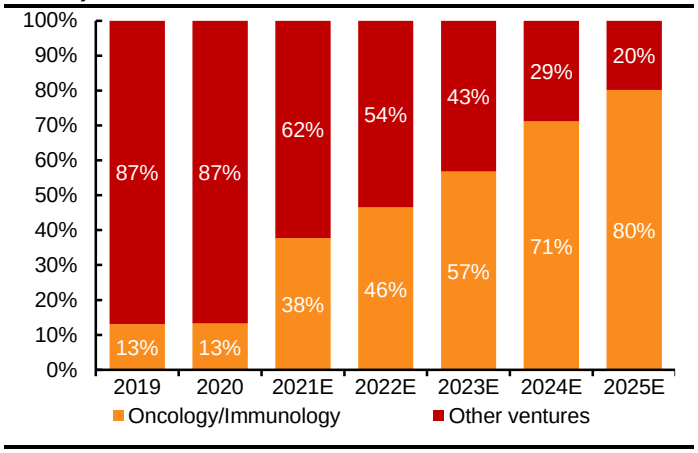
We forecast total revenue to reach US$340mn/ US$423mn/ US$561mn in FY21E/22E/23E, representing a YoY change of 49%/ 25%/ 33%, respectively. For Oncology/ Immunology segment, we forecast US$128mn/ US$197mn/ US$319mn in revenue in FY21E/22E/23E, representing respective YoY growth of 325%/ 53%/ 62%, mainly driven by sales ramp-up of savolitinib, fruquintinib and surufatinib. For Other Venture segment, we assume a CAGR of 7% over FY21-23E and project US$212mn/ US$226mn/ US$242mn in revenue in FY21E/ 22E/ 23E, respectively.

Figure 77: Total revenue forecast by segment (2019-2025E)



Source: Company data, CMBIS estimates

Figure 78: Total revenue breakdown by segment (2019-2025E)



Source: Company data, CMBIS estimates

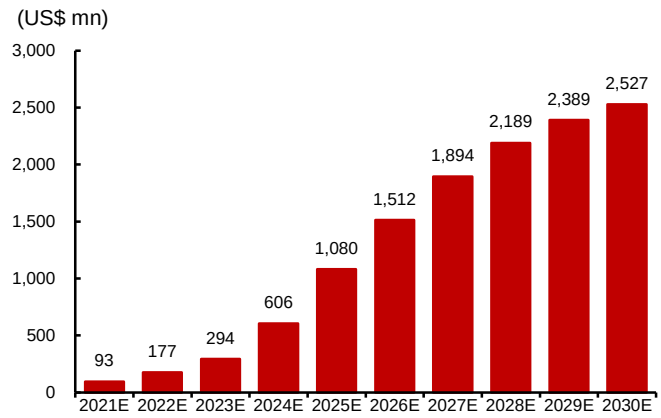
Figure 79: Innovative drug revenue forecast (2021E-2030E)

(YE 31 Dec) (US$ mn)	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Savolitinib	15	24	42	95	135	190	235	271	302	322
YoY		*63%*	*75%*	*124%*	*42%*	*40%*	*24%*	*16%*	*11%*	*7%*
Fruquintinib	60	77	95	250	453	656	840	951	1,030	1,067
YoY		*30%*	*22%*	*164%*	*81%*	*45%*	*28%*	*13%*	*8%*	*4%*
Surufatinib	19	75	157	260	471	640	764	877	933	978
YoY		*299%*	*109%*	*66%*	*81%*	*36%*	*19%*	*15%*	*6%*	*5%*
HMPL689					10	13	23	35	51	66
YoY						*30%*	*74%*	*56%*	*45%*	*29%*
HMPL623					2	4	9	15	23	34
YoY						*103%*	*124%*	*77%*	*55%*	*43%*
Tazemetostat					9	10	15	20	23	25
YoY						*12%*	*54%*	*35%*	*12%*	*11%*

Other products							10	18	26	34
YoY								*80%*	*44%*	*31%*
Innovative drug revenue	**93**	**177**	**294**	**606**	**1,080**	**1,512**	**1,894**	**2,189**	**2,389**	**2,527**
YoY		*89%*	*66%*	*106%*	*78%*	*40%*	*25%*	*16%*	*9%*	*6%*

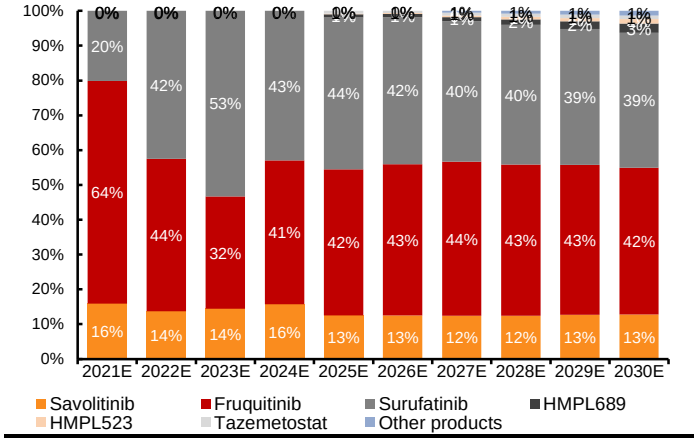
Source: Company data, CMBIS estimates

Figure 80: Innovative drug revenue (2021E-2030E)



Source: Company data, CMBIS estimates

Figure 81: Innovative drug revenue mix (2021E-2030E)



Source: Company data, CMBIS estimates

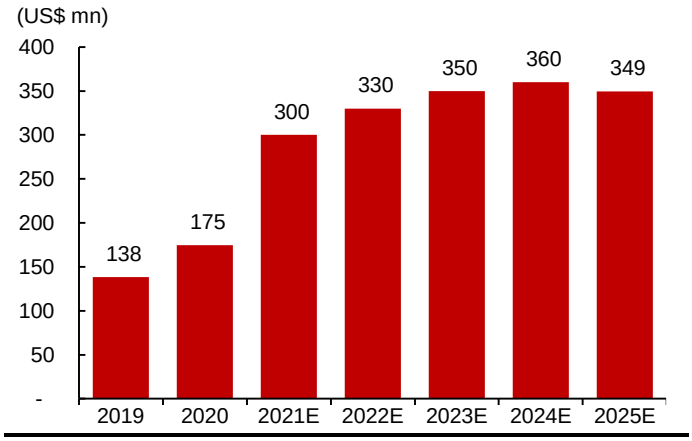
HCM incurred attributable net loss of US$106mn/ US$126mn/ US$102mn in 2019/ 2020/ 1H21. We project continued attributable net loss of US$220mn/ US$277mn/ US$225mn in FY21E/ 22E/ 23E, respectively.

Figure 82: P&L forecasts (2019-2025E)

(US$ mn)	2019	2020	2021E	2022E	2023E	2024E	2025E
Revenue	205	228	340	423	561	900	1,397
YoY		*11%*	*49%*	*25%*	*33%*	*60%*	*55%*
Gross profit	45	39	114	158	248	475	816
GPM	*22%*	*17%*	*34%*	*37%*	*44%*	*53%*	*58%*
R&D expenses	(138)	(175)	(300)	(330)	(350)	(360)	(349)
% of revenue	*-67%*	*-77%*	*-88%*	*-78%*	*-62%*	*-40%*	*-25%*
Selling expenses	(14)	(11)	(55)	(59)	(67)	(90)	(137)
% of revenue	*-7%*	*-5%*	*-16%*	*-14%*	*-12%*	*-10%*	*-10%*
Administrative expenses	(39)	(50)	(70)	(75)	(80)	(90)	(126)
% of revenue	*-19%*	*-22%*	*-21%*	*-18%*	*-14%*	*-10%*	*-9%*
Operating profit	(146)	(197)	(311)	(306)	(249)	(65)	204
Other income, net	5	7	7	5	(0)	(3)	(3)
% of revenue	*3%*	*3%*	*2%*	*1%*	*0%*	*0%*	*0%*
Profit (loss) before tax	(141)	(190)	(304)	(301)	(249)	(68)	201
Income tax	(3)	(5)	-	-	-	-	(30)
% tax rate	*2%*	*3%*	*0%*	*0%*	*0%*	*0%*	*-15%*
Equity in earnings of equity investees, net of tax	41	79	90	30	30	30	30
Profit (loss) for the year	(104)	(116)	(214)	(271)	(219)	(38)	201
Minority interests	(2)	(10)	(6)	(6)	(6)	(6)	(6)
Profit (loss) attributable to shareholders	(106)	(126)	(220)	(277)	(225)	(44)	195

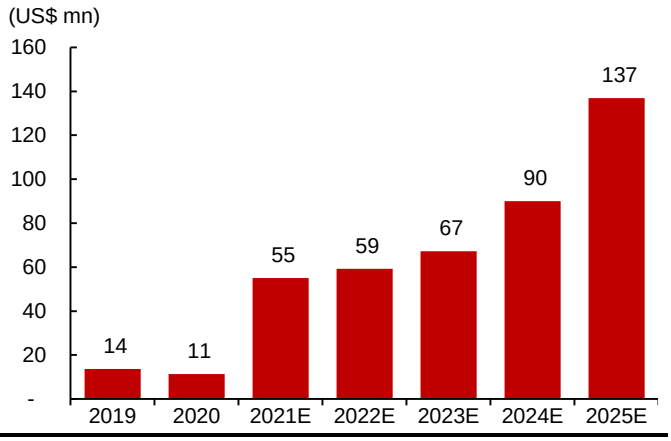
Source: Company data, CMBIS estimates

Figure 83: R&D expense forecast (2019-2025E)



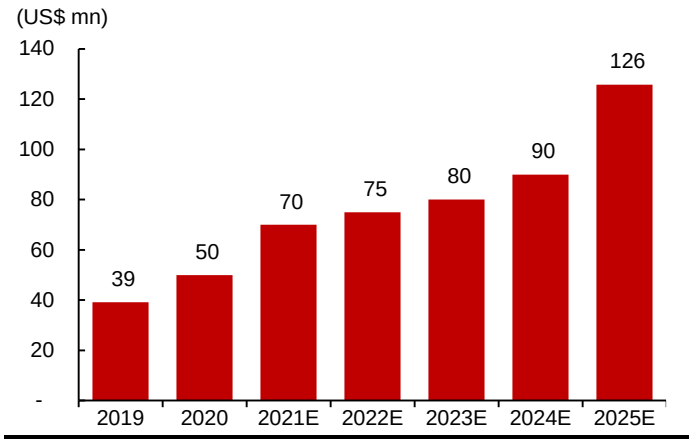
Source: Company data, CMBIS estimates

Figure 84: Selling expense forecast (2019-2025E)



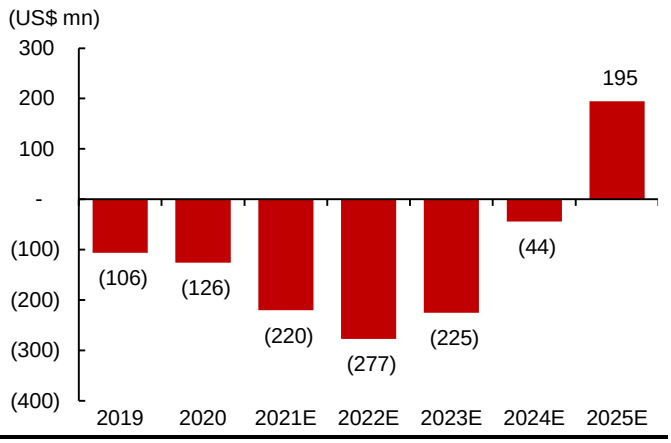
Source: Company data, CMBIS estimates

Figure 85: Administrative expense forecast (2019-2025E)



Source: Company data, CMBIS estimates

Figure 86: Net profit forecast (2019-2025E)



Source: Company data, CMBIS estimates

Valuation

Initiate at BUY with TP of HK$77.74

We derive our target price of HK$77.74 based on a 15-year DCF valuation (WACC: 9.07%, terminal growth rate: 4.0%). We expect HCM to generate positive free cash flows starting FY2025.

Figure 87: Risk-adjusted DCF valuation

DCF Valuation (in US$ mn)	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	(308)	(303)	(246)	(62)	207	405	644	883	1,110	1,214	1,271	1,309	1,176	1,187	1,199
Tax rate	0%	0%	0%	0%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
EBIT*(1-tax rate)	(308)	(303)	(246)	(62)	176	344	547	751	943	1,032	1,081	1,113	999	1,009	1,020
+ D&A	5	11	19	17	16	14	14	13	12	12	11	11	11	11	11
- Change in working capital	(0)	(20)	(15)	(30)	(64)	(87)	(71)	(70)	(55)	(42)	(27)	(15)	(1)	43	(1)
- Capex	(35)	(50)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
FCFF	**(338)**	**(362)**	**(252)**	**(85)**	**117**	**262**	**480**	**684**	**891**	**992**	**1,055**	**1,099**	**1,000**	**1,053**	**1,019**
Terminal value															**20,886**

Present value of enterprise (US$ mn)	8,171
Net debt (US$ mn)	(500)
Equity value (US$ mn)	8,671
Equity value (HK$ mn)	67,175
No. of outstanding shares (mn)	864
DCF per share (HK$)	**77.74**
Terminal growth rate	**4.0%**
WACC	**9.07%**
Cost of Equity	11.5%
Cost of Debt	4.0%
Equity Beta	0.81
Risk Free Rate	3.0%
Market Risk Premium	10.5%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%

Source: CMBIS estimates

Figure 88: Sensitivity analysis

		WACC				
		8.07%	**8.57%**	**9.07%**	**9.57%**	**10.07%**
Terminal growth rate	**3.00%**	87.66	77.43	68.95	61.82	55.75
	3.50%	94.30	82.54	72.95	65.00	58.31
	4.00%	102.57	88.76	**77.74**	68.75	61.30
	4.50%	113.15	96.51	83.57	73.24	64.82
	5.00%	127.17	106.43	90.84	78.72	69.03

Source: CMBIS estimates

Figure 89: Peers valuation table

Company	Ticker	Rating	Current Price (HK$)	Target Price (HK$)	Mkt cap HK$mn	PS(x) FY21E	PS(x) FY22E
HUTCHMED	**13 HK**	**BUY**	**59.70**	**77.74**	51,603	**19.6**	**15.7**
BeiGene	6160 HK	N/A	231.60	NR	280,117	31.1	25.5
Zai Lab	9688 HK	N/A	985.00	NR	93,978	81.9	36.0
Innovent	1801HK	BUY	61.10	116.89	89,118	17.2	11.1
Junshi	1877 HK	N/A	41.20	NR	56,669	11.3	12.1
RemeGene	9995 HK	N/A	96.80	NR	47,416	48.3	30.5
Akeso	9926 HK	N/A	40.90	NR	33,418	61.3	17.8
Kintor	9939 HK	BUY	74.80	98.07	28,992	607.7	1.7
Innocare	9969 HK	BUY	19.24	24.66	28,854	23.4	38.6
Alphamab	9966 HK	N/A	20.40	NR	19,091	229.7	76.4
Everest	1952 HK	N/A	60.55	NR	18,030	1997.6	58.6
Jacobio	1167 HK	N/A	21.50	NR	16,586	51.2	34.2
CStone	2616 HK	N/A	12.08	NR	14,301	43.7	11.7
Henlius	2696 HK	BUY	25.10	60.61	13,642	6.9	3.9
Ascentage	6855 HK	BUY	34.50	67.20	9,084	77.1	21.4

Source: Bloomberg (as of Sep 16, 2021), CMBIS

Financial Summary

Income statement

YE Dec 31 (US$ mn)	FY19A	FY20A	FY21E	FY22E	FY23E
Revenue	**205**	**228**	**340**	**423**	**561**
COGS	(160)	(189)	(226)	(265)	(312)
Gross profit	**45**	**39**	**114**	**158**	**248**
Administrative expenses	(39)	(50)	(70)	(75)	(80)
R&D expenses	(138)	(175)	(300)	(330)	(350)
Selling expenses	(14)	(11)	(55)	(59)	(67)
Operating profit	**(146)**	**(197)**	**(311)**	**(306)**	**(249)**
Interest income	5	3	5	5	2
Other income (expenses), net	2	5	3	3	3
Interest expense	(1)	(1)	(1)	(3)	(6)
Other expense	(0)	(0)	0	0	0
Pre-tax profit	**(141)**	**(190)**	**(304)**	**(301)**	**(249)**
Income tax	(3)	(5)	0	0	0
Equity in earnings of equity investees, net of tax	41	79	90	30	30
Minority interests	(2)	(10)	(6)	(6)	(6)
Net profit (loss)	**(106)**	**(126)**	**(220)**	**(277)**	**(225)**

Cash flow summary

YE Dec 31 (US$ mn)	FY19A	FY20A	FY21E	FY22E	FY23E
Profit before tax	**(104)**	**(116)**	**(214)**	**(271)**	**(219)**
Depreciation and amortization	5	6	5	11	19
Change in working capital	16	29	(0)	(20)	(15)
Changes in income tax balances	0	(1)	0	0	0
Others	1	19	(90)	(30)	(30)
Net cash from operating	**(81)**	**(62)**	**(300)**	**(310)**	**(245)**
Capex	(9)	(8)	(35)	(50)	(10)
Net proceeds from disposal of short-term investments	(478)	(733)	0	0	0
Other investing activities	606	615	0	0	0
Net cash from investing	**119**	**(125)**	**(35)**	**(50)**	**(10)**
Net proceeds from shares issued	0	319	635	0	0
Net bank borrowing	(0)	0	0	100	100
Other financing activities	(2)	(23)	0	0	0
Net cash from financing	**(1)**	**296**	**635**	**100**	**100**
FX changes	(2)	6	0	0	0
Net change in cash	**37**	**109**	**300**	**(260)**	**(155)**
Cash at the beginning of the year	86	121	236	536	276
Cash at the end of the year	**121**	**236**	**536**	**276**	**121**

Balance sheet

YE Dec 31 (US$ mn)	FY19A	FY20A	FY21E	FY22E	FY23E
Non-current assets	**148**	**193**	**314**	**383**	**404**
PP&E	21	24	54	93	85
Right-of-use assets	6	8	8	ss8	8
Deferred tax assets	1	2	2	2	2
Investments in equity investees	16	0	0	0	0
Other non-current assets	22	20	20	20	20
Current assets	**317**	**531**	**831**	**597**	**463**
ssCash and cash equivalen	121	236	536	276	121
Short-term investments	96	200	200	200	200
Accounts receivable	43	48	46	68	85
Inventories	16	20	22	25	30
Other current assets	40	28	28	28	28
Current liabilities	**113**	**158**	**158**	**164**	**170**
Accounts payable	24	32	31	37	44
Other payables, accruals and advance receipts	82	121	121	121	121
Lease liabilities	3	3	3	3	3
Other current liabilities	4	4	4	4	4
Non-current liabilities	**39**	**47**	**47**	**147**	**247**
Lease liabilities	3	6	6	6	6
Long-term bank borrowings	27	27	27	127	227
Other non-current liabilities	9	14	14	14	14
Total net assets	**313**	**519**	**940**	**669**	**450**
Minority interest	(2)	(10)	(6)	(6)	(6)
Shareholders' equity	**313**	**519**	**940**	**669**	**450**

Key ratios

YE 31 Dec	FY19A	FY20A	FY21E	FY22E	FY23E
Profit & loss ratios (%)					
Gross margin	22	17	34	37	44
EBITDA margin	(68)	(82)	(89)	(69)	(41)
Net margin	(52)	(55)	(65)	(65)	(40)
Effective tax rate (%)	N/A	N/A	N/A	N/A	N/A
Balance sheet ratios					
Current ratio (x)	3	3	5	4	3
Inventory days					
Account receivables turnover	73	70	70	70	70
Account receivables turnover	4	2	3	3	3
Account payables turnover days	57	54	60	60	60
Total debt to asset ratio (%)	29	28	18	32	48
Returns (%)					
ROE	(33)	(22)	(23)	(41)	(49)
ROA	(19)	(16)	(19)	(28)	(25)
Per share data					
EPS (USD)	(0.2)	(0.2)	(0.3)	(0.3)	(0.3)
DPS (USD)	0.0	0.0	0.0	0.0	0.0
BVPS (USD)	0.5	0.7	1.1	0.8	0.5

Source: Company data, CMBIS estimates

Investment risks

1) Clinical development risks

Positive early study results may not be predictive of later-stage trial's success. Any failure in HCM's pipeline's ongoing trials may potentially result in failure in product approval.

2) Regulatory approval risks

The Company's ability to generate revenue will depend primarily on the successful regulatory approvals of its pipeline assets.

3) Competition risk

The Company may be exposed to fierce competition as competitors may develop and commercialize drugs ahead of the curve leading to market saturation.

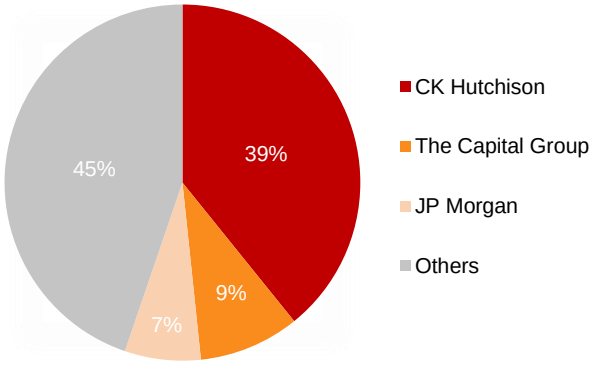
Appendix

Figure 90: Upcoming catalysts

Drug	Treatment type	Indication	Event	Time	Impact
Savolitinib	Mono	MET+ NSCLC	China: potential inclusion in 2022 NRDL	2H21	High
Surufatinib	Mono	pNET; npNET	China: potential inclusion in 2022 NRDL	2H21	High
Tazemetostat	Combo+Rituximab and Lenalidomide, followed by Tazemetostat	2L FL	China: Discussion with CDE on trial design and to join global Phase III trial	2H21	High
Savolitinib	Combo+Tagrisso	2L EGFRm+ TKI refractory MET+ NSCLC	China: to initiate Phase III trial	2H21	Mid
Savolitinib	Combo+Tagrisso	2L/3L EGFRm+ (Tagrisso refractory) MET+ NSCLC	Global: to initiate Phase III trial	2H21	Mid
Savolitinib	combo+IMFINZI	MET+ PRCC	Global: to start patient enrollment of Phase III trial	2H21	Mid
Surufatinib	Combo+JS001	Neuroendocrine carcinoma (NEC)	China: to initiate Phase III trial	2H21	Mid
Fruquintinib	Combo+sintilimab	Endometrial cancer	China: to initiate Phase III trial	2H21	Mid
Fruquintinib	Mono	3L CRC	US/EU/Japan: to complete patient enrollment of Phase III trial	2H21	Mid
HMPL-689	Mono	Indolent NHL	US/EU: to engage with regulatory authorities on discussion potential registration pathway	2H21	Mid
HMPL-689	Mono	Indolent NHL	China: to present expansion data at ESMO	2H21	Mid
HMPL-523	Mono	2L ITP	China: to initiate Phase III trial	2H21	Mid
HMPL-306	Mono	Hematological malignancies	China: to complete Phase I dose escalation study	2H21	low
HMPL-306	Mono	Solid tumors	US/EU: to complete Phase I dose escalation study	2H21	low
HMPL-760*	TBD	Hematological malignancies	US: targeting PFI	2H21	Low
HMPL-760*	TBD	Hematological malignancies	China: targeting PFI	2H21	Low
HMPL-653^	TBD	Solid tumors	China: potential IND submission to NMPA	2H21	Low
HMPL-A83**	TBD	Hematological malignancies	China: potential IND submission to NMPA	2H21	Low
HMPL-A83**	TBD	Hematological malignancies	US: potential IND submission to FDA	2H21	Low
Surufatinib	Mono	NETs	US: potential NDA approval by FDA	1H22	High
Surufatinib	Mono	NETs	EU: potential MAA approval by EMA	1H22	High
Surufatinib	Combo+JS001	GC/GEJ	China: discussion on registration design and potential start of Phase III trial	1H22	Mid
Fruquintinib	Combo+Paclitaxel	2L GC	China: expected topline Phase III data readouts and potential NDA submission	2H22	Mid

Source: Company data, CMBIS; Note: HMPL-760*: 3rd - generation BTK inhibitor; HMPL-653^: CSF-1R inhibitor; HMPL-A83**: CD47mAb

Figure 91: Shareholding structure of HCM (as of Sep 2021)



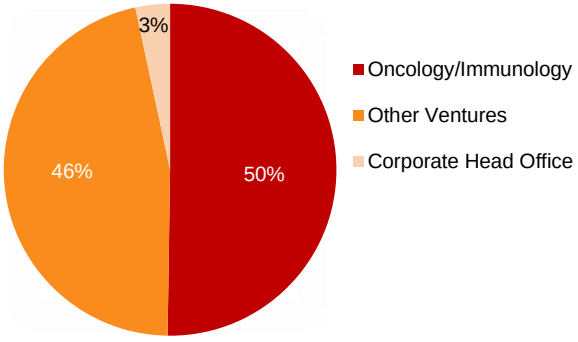
Source: Company data, CMBIS

Figure 92: Employee structure (as of 31 Dec 2020)

Function	# of employees	% of Total
Oncology/Immunology	643	50%
Other Ventures	594	46%
Corporate Head Office	43	3%
Total	**1,280**	**100%**

Source: Company data, CMBIS

Figure 93: Employee breakdown (as of 31 Dec 2020)



Source: Company data, CMBIS

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