

# Hutchison China MediTech

Jewels in the crown

Corporate update

Pharma & biotech

**Key near-term value drivers include newsflow from partnered assets savolitinib (AZN globally) and fruquintinib (LLY in China). By year end, we anticipate the China FDA to approve fruquintinib (3L CRC). The molecular epidemiology study (MES) data on savolitinib in PRCC could support a US NDA submission (possible breakthrough therapy designation, BTD). Both products have blockbuster potential; as combination therapies in cancer drive overall uptake of targeted therapies. Beyond this we expect progression in Hutchison China MediTech's (HCM) wholly owned late stage oncology assets to reach value inflection points over the next few years. We have extensively reviewed our financial forecasts and increase our valuation to £71.0/share or \$6.4bn.**

Year end	Revenue (US\$m)	Net profit* (US\$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/16	216.1	11.7	19.6	0.0	293	N/A
12/17	241.2	(26.7)	(43.3)	0.0	N/A	N/A
12/18e	163.6	(41.3)	(62.1)	0.0	N/A	N/A
12/19e	180.1	(62.2)	(93.5)	0.0	N/A	N/A

Note: \*Net profit and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

## Innovation platform approaching commercialisation

We expect fruquintinib to be approved and launched in China (Colorectal Cancer) late 2018. Savolitinib's potential US approval for PRCC and launch by partner AstraZeneca would be of great significance as the first internally developed HCM asset to launch worldwide. We have increased our peak sales forecasts for both; driven by the opportunities in non-small cell lung cancer (NSCLC) where multiple positive combination data readouts from savolitinib and fruquintinib highlight a widening of the eligible patient population that can receive these treatments.

## Wholly owned assets coming to the spotlight

Data from rest of the pipeline will provide further inflection points in 2019/20. We previously assumed that HCM would partner all assets. However, with its growth in expertise and increased financial strength, we forecast that HCM will develop the global footprint in key markets to launch these products alone. Our analysis concludes that much higher economic value resides in this strategy in particular with respect to fruquintinib (ex-China), sulfatinib, epitinib, and thelatinib. We expect HCM to become a major China and international oncology company.

## Valuation: \$6.4bn (£71.0/share, \$47.9/ADS)

Our large uplift in valuation stems from multiple factors. Our peak sales for savolitinib and fruquintinib benefit from the above-mentioned factors. Changing the economic terms for wholly owned assets has a disproportionate impact given these products could reach much higher operating margins than our prior flat 30% royalty rate on sales assumption. We also incorporate a terminal value for the first time to reflect the maturity of the company and depth of the pipeline to our higher sum-of-the-parts (SOTP) valuation of \$6.4bn or £71.0/share (vs \$2.7bn, or £36.1/share, in June 2017).

31 May 2018

**Price** 4,260p

**Market cap** £2,833m

\$1.35/£

Net cash (\$m) at 31 December 2017 328.3

Shares in issue 66.5m

Free float 37%

Code HCM

Primary exchange AIM

Secondary exchange NASDAQ

## Share price performance



% 1m 3m 12m

Abs (11.3) (10.3) 35.8

Rel (local) (13.3) (15.5) 32.3

52-week high/low 5,890.0p 3,087.5p

## Business description

Hutchison China MediTech is an innovative China-based biopharmaceutical company targeting the global market for novel, highly selective oral oncology and immunology drugs. Its established commercial platform business in China is growing ahead of the market.

## Next events

Fruquintinib China NDA approval and launch in CRC H218

Fruquintinib FALUCA top-line data 2018

Savolitinib MES data Late 2018

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**Hutchison China MediTech is a research client of Edison Investment Research Limited**

## Investment summary

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### Multiple factors drive upgrade

We anticipate 2018/19 to be a transformative period for HCM. Its first internally developed TKI fruquintinib (third-line CRC) could be approved by the China FDA (NDA submitted mid-2017) during 2018 and launched later in the year. Savolitinib's and fruquintinib's Phase III programmes (in combination and as monotherapies) across multiple cancer indications could continue to widen the eligible patient populations for these compounds, driving significant upgrades to our numbers. However, the clear risk is failure of Phase III trials of one or more assets. HCM now has a total of eight clinical-stage assets and a number of second-generation immunotherapy compounds moving towards entering the clinic. With its burgeoning number of wholly owned, late-stage assets, we now forecast HCM to initiate a global footprint to launch these products alone, particularly if a number of these assets do make it to market. Our analysis concludes that much higher economic value resides in this strategy given the requirements for a specialist oncology salesforce in addition to clinical and regulatory infrastructure in key markets. While our expectations for the value of the pipeline have increased and, although our risk-adjusted NPV highlights the future sources of upside to the shares, the failure of one or more products would have a negative effect on the shares, particularly the main contributors to our valuation: savolitinib, fruquintinib, sulfatinib and epitinib. HCM's profitable Chinese healthcare commercial business (CP) continues to benefit from the fast-growing domestic market; cash generated from CP continues to be reinvested in developing the burgeoning IP pipeline. For more information on the company's full portfolio, see our note [Stellar Evolution](#), published in May 2016.

### Valuation: \$6.4bn (£71.0/share, \$47.9/ADS)

We have significantly increased our SOTP valuation (Exhibit 1) to \$6.4bn or £71.0/share (vs \$2.7bn, or £36.1/share in June 2017). The major sources of uplift are: 1) increased peak sales forecasts for savolitinib and fruquintinib in NSCLC, driven by the significant combination opportunities that exist in this indication; 2) changing the economic terms for wholly owned assets (fruquintinib ex-China, and globally for sulfatinib, epitinib, theliatinib, HMPL-523) from our prior flat 30% royalty rate on sales assumption to full value retained by HCM (we decrease peak sales for these assets and now reflect product operating expenses relating to sales and marketing and infrastructure costs); and 3) introduction of a terminal value for the first time to reflect the maturity of the company and depth of the rest of the pipeline. FY17 was punctuated by multiple positive clinical data points and a gross \$301.3m equity raise. We have updated our model for FY17 results, rolled forward our DCF and updated our probabilities of success for assets that have progressed and have pushed back some launch dates by 1-2 years. We value the Innovation Platform (IP) at \$4,702.6m and placing the Commercial Platform's (CP) 2018e share of net profit on a 20.4x rating gives \$848.2m (945p/share). Adding in December 2017 net cash results in a value of \$6.4bn or £71.0/share.

Our key product considerations for our valuation upgrades are:

- **Savolitinib Tagrisso/Iressa combination data NSCLC** (World Conference on Lung Cancer, WCLC, 2017): the significant increase in our savolitinib valuation is driven largely by higher penetration rates in NSCLC across all regions. Combination data presented at WCLC further validate c-Met as a target in NSCLC and savolitinib as a drug candidate, notably in combination with either Tagrisso or Iressa. We anticipate savolitinib will be used as monotherapy in first line and now expect it to be used in combination with Tagrisso in second- and third-line patients in the EU and US and in second-line patients with Iressa in China. We have also increased our probability of success to 75% (from 50%).

- **Fruquintinib Iressa first-line combination NSCLC** (WCLC 2017): positive preliminary data presented at WCLC 2017 from an ongoing Phase II trial testing fruquintinib (VEGFR inhibitor) in combination with Iressa in first-line EGFR-mutant NSCLC support this unique VEGFR inhibitor's role in combination therapy. Critically, our revised NSCLC numbers take into consideration fruquintinib use in earlier lines of treatment as combination therapy in addition to our original assumption of its use as monotherapy in third line treatment. We increase our China pricing assumption for fruquintinib to \$3,500 per month (from \$2,500).
- **Fruquintinib FRESCO data CRC** (ASCO 2017): FRESCO data underpin the hypothesis that fruquintinib's safety and efficacy profile could enable it to be positioned as best-in-class in China. HCM and partner Lilly submitted the NDA for third-line CRC to the China FDA in June 2017 and we anticipate fruquintinib launch in China in 2018. We have increased its probability of success to 90% from our original 75%.
- **Wholly owned assets: Epirutinib NSCLC with brain metastasis** phase III trial in China has started enrolling patients and we increase its probability of success to 75% from our original 30%. We introduce additional indications for sulfatinib (biliary tract ca.) and HMPL 523 (haematological cancers).
- Changing the economic terms for wholly owned assets (fruquintinib ex-China, and globally for sulfatinib, epirutinib, thelirutinib. HMPL 523) from our prior flat 30% royalty rate on sales assumption to full value retained by HCM (we decrease peak sales for these assets and now reflect product operating expenses relating to sales and marketing and infrastructure costs).
- Additionally, some of HCM's second wave of innovation candidates (HMPL-689 and HMPL-453) contributes little or nothing to our valuation. Progress to proof of concept (POC) for these assets would increase our risk-adjusted valuation.

Exhibit 1: HCM valuation										
Product	Indication	Launch	Peak sales (\$m)	Value (\$m)	Probability	rNPV (\$m)	rNPV/share (\$/share)	rNPV per share (£)	rNPV/ADS (\$/ADS)	NPV* per share £
Savolitinib (AZD6094/volitinib)	Papillary renal cell carcinoma	2020 (China) 2021 (ROW)	\$64m (China) \$267m (ROW)	203.5	75%	152.0	2.3	1.7	1.1	2.3
	Clear cell carcinoma	2022 (China) 2022 (ROW)	\$169m (China) \$987m (ROW)	310.3	35%	107.0	1.6	1.2	0.8	3.5
	NSCLC	2021 (China) 2021 (ROW)	\$387m (China) \$2.5bn (ROW)	815.3	75%	611.4	9.2	6.8	4.6	9.1
	Gastric Ca	2022 (China) 2023 (ROW)	\$326m (China) \$750m (ROW)	336.8	35%	115.4	1.7	1.3	0.9	3.8
	Pulmonary sarcomatoid ca	2021 (Global))	\$476m (Global)	359.6	50%	178.8	2.7	2.0	1.3	4.0
Fruquintinib	CRC	2018 (China) 2022 (ROW)	\$149m (China) \$565m (ROW)	772.3	90%	695.1	10.4	7.7	5.2	8.6
	NSCLC	2020 (China) 2021 (ROW)	\$334m (China) \$721m (ROW)	1,090.4	75%	817.8	12.3	9.1	6.1	12.1
	Gastric Ca	2020 (China) 2022 (ROW)	\$292m (China) \$392m (ROW)	713.1	75%	534.8	8.0	6.0	4.0	7.9
Sulfatinib	NET	2021 (China) 2021 (ROW)	\$79m (China) \$454m (ROW)	841.6	75%	631.2	9.5	7.0	4.7	9.4
	Thyroid ca	2021 (China) 2022 (ROW)	\$72m (China) \$212m (ROW)	279.3	50%	139.7	2.1	1.6	1.0	3.1
	Biliary Tract	2023 (China) 2023 (ROW)	\$190m (China) \$137m (ROW)	344.0	50%	165.5	2.5	1.8	1.2	3.8
Epitinib	NSCLC	2021 (China) 2022 (ROW)	\$198m (China) \$212m (ROW)	520.7	75%	390.5	5.9	4.3	2.9	5.8
Theliatinib	Oesophageal ca	2022 (China) 2022 (ROW)	\$328m (China) \$129m (ROW)	618.1	10%	61.8	0.9	0.7	0.5	6.9
HMPL-523	RA	2023 (WW)	\$1.6bn (Global)	801.5	10%	80.1	1.2	0.9	0.6	8.9
	Haematological cancers	2023 (WW)	\$95m (China) \$86m (ROW)	121.5	30%	21.5	0.3	0.2	0.2	1.4
<b>Valuation of IP only</b>				<b>\$8,128.0</b>		<b>\$4,702.6</b>	<b>\$70.70</b>	<b>£52.37</b>	<b>\$35.35</b>	<b>£90.52</b>
CP				848.2	100%	848.2	12.75	9.45	6.38	9.4
<b>Net cash December 2017</b>				<b>328.3</b>	<b>100%</b>	<b>328.3</b>	<b>4.9</b>	<b>3.66</b>	<b>2.47</b>	<b>3.7</b>
Terminal value				491.8	100%	491.8	7.4	5.48	3.70	5.5
<b>Valuation</b>				<b>\$9,796.3</b>		<b>\$6,370.9</b>	<b>\$95.8</b>	<b>£70.95</b>	<b>\$47.89</b>	<b>£109.09</b>

Source: Edison Investment Research. Note: \*Non-risk adjusted NPV per share assumes 100% probability of success. \*\*Probability reflects likely filing with Phase II data for BT. FX rate \$1.35/£. Number of shares outstanding 66.52m. Ca.= cancer

## Sensitivities: limited free float reduces the shares' liquidity

HCM is subject to the usual biotech and drug development risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. Expectations for the pipeline have increased and, although our risk-adjusted NPV highlights the future sources of upside to the shares, the failure of one or more products would have a negative effect on the shares, particularly the main contributors to our valuation, savolitinib, fruquintinib, sulfatinib and epitinib. CK Hutchison's involvement in HCM means investors are minority shareholders. Additionally, the limited free float reduces the shares' liquidity.

## Financials: Cash bolstered by secondary ADR issuance

Full-year 2017 results published in March 2018 highlighted robust growth within the profitable China commercial platform (CP) division, coupled with clinical progress within the IP portfolio. HCM reported a healthy cash position with available cash resources of \$479.6m (at 31 December) at the group level (cash and cash equivalents including short-term investments of \$358.3m, and unutilised bank borrowing facilities of \$121.3m). In October 2017 HCM raised \$301.3m (gross) (net \$292.7m) in new equity capital via a follow-on offering on NASDAQ. This combined with the substantial cash generation from the CP division means that HCM is well funded through to approvals of multiple drugs in 2020/21 timeframe taking into account the considerable increase in R&D expenses in 2018 and 2019. Full-year 2018 revenue guidance for the group of \$155-175m reflect in part changes to

the sales model relating to the new CFDA two-invoice system roll out in China; while gross revenue amounts are affected, overall profit contribution from these business activities substantially remain unchanged. Guidance for 2018 stands at a net loss of \$19-52m at the group level; this reflects an increase in R&D expenses (adjusted non-US GAAP \$110-120m) as the pipeline continues to mature. Variance in net income reflects unknown timing of one-time property gains (guidance \$0-20m) from Guangzhou land – the timing of this is subject to Guangzhou government policy.

## 2018 to be defined by first approval

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FY17 was defining for HCM's late-stage TKI portfolio. Data presented at a number of conferences (including ASCO GI 2017, ASCO GU 2017 and WCLC 2017) on savolitinib and fruquintinib led to a re-rating of the shares as investor confidence increased on HCM's R&D strategy. Furthermore, data on compounds being developed by its peers highlight the fast-moving treatment paradigms in oncology (eg AZN's Tagrisso FLAURA data could enable approval in 1L in all EGFRm-positive NSCLC) and the importance of using combination drugs to create synergistic efficacy in resistance cancer subtypes. This bodes well for HCM's strategy to develop best-in-class products with potential to be used as monotherapy and combination strategy. HCM's partnership with AstraZeneca (AZN) gives it access to AZN's EGFR/T790M inhibitors Iressa and Tagrisso; discussions and planning are ongoing with AZN on pivotal savolitinib combination studies. Savolitinib's and fruquintinib's Phase III programmes (in combination and as monotherapies) across multiple cancer indications continue to widen the eligible patient populations for these compounds, driving significant upgrades to our numbers.

HCM now has a total of eight clinical-stage assets and a number of second-generation immunotherapy compounds moving towards entering the clinic. The importance of this is HCM could have a portfolio of oncology drugs to launch in the 2019-2021 timeframe; this includes fruquintinib ex-China (we assume Lilly does not take its optionality) and the wholly owned, late-stage oncology assets (sulfatinib, epitinib, theliatinib). Previously we had anticipated HCM to seek partnering for assets at the phase II stage in return for royalty on sales. For international markets ex-China we now expect that HCM will build its commercial footprint in key markets in order to leverage the multiple assets that could be approved from 2020. In China we expect HCM to capitalise on its substantial China-based commercial presence by launching its wholly owned assets into the domestic market through its CP division.

We anticipate significant operational leverage in the medium term from the two platforms; this would serve as a major source of uplift in economic returns.

### Key catalysts in 2018

We expect the CFDA to approve fruquintinib in third-line CRC later this year; approval would validate the R&D innovation strategy at HCM. We remain positive on HCM's TKI pipeline, efficacy and tolerability data presented across multiple savolitinib and fruquintinib trials (monotherapies and in combination with agents such as chemotherapies, targeted therapies, and immunotherapies) have led to a reassessment of some of our core assumptions for these assets. Combination EGFR therapy is being used increasingly to treat refractory NSCLC patients, which is opening new treatment paradigms. We anticipate savolitinib and fruquintinib use higher up in the lung cancer treatment algorithm as monotherapy and in combination. Exhibit 2 highlights the key milestones expected in 2018.

**Exhibit 2: Potential key milestones for 2018**

Product	Indication	Next news
Savolitinib	Papillary renal cell carcinoma	Molecular epidemiology study (n>300) in papillary renal cell carcinoma – possible BTD-enabling.
	NSCLC	Initiation of a global Phase III pivotal study in second-line NSCLC in combination with Tagrisso (randomised, chemo-doublet controlled). AZN/HCM decision on strategy for global Phase III pivotal study in third-line NSCLC in combination with Tagrisso. AZN/HCM decision on China Phase III pivotal study in second-line NSCLC in combination with Iressa.
Fruquintinib	CRC	China NDA approval (third-line CRC) and launch (contingent on approval).
	NSCLC	China Phase III (FALUCA) top-line data (third-line monotherapy).
Epitinib	NSCLC with brain metastases	Initiate China Phase III first-line EGFRm NSCLC with brain metastases.
Sulfatinib	Neuro endocrine tumours	Initiate US Phase IIa expansion study in neuro endocrine tumours and solid tumours.
HMPL-523	Cancer	Initiate dose expansion proof-of-concept studies in haematological cancer in both Australia and China. Potential presentation of preliminary efficacy and safety data from Phase I/Ib dose escalation/expansion studies in haematological cancer.
HMPL-689	Cancer	Initiate Phase Ib expansion studies in China in haematological cancer patients. Present Phase I dose escalation data in Australian healthy volunteers.

Source: Company presentations, Edison Investment Research

The first section of this note discusses key assets savolitinib and fruquintinib. Both have progressed through 2017 and we detail clinical trial data published throughout the year and the status of ongoing trials through the different oncology indications. The second part of the note focuses on the China and international strategy for the product portfolio. Last, in the valuation section we discuss the implications of all of this on our higher valuation of the company.

## Savolitinib shines brightly in combinations

Savolitinib is a selective small molecule c-Met inhibitor and its advancement through to Phase III clinical trials continues to validate c-Met as a target. Presently there are no selective c-Met inhibitors commercially approved; however, interest in c-Met as a target has grown significantly in the past few years and global pharmaceutical companies are taking interest given savolitinib's blockbuster potential. The most advanced of these competitors are capmatinib (Novartis/Incyte) in Phase III development in NSCLC and tepotinib (Merck Serono) in Phase II development in NSCLC and hepatocellular carcinoma.

Savolitinib is advancing in a number of MET-driven solid cancer indications. In our view it is well placed to be best-in-class and potentially first-in-class (capmatinib may be first to market in NSCLC) across a range of MET-driven cancers. We anticipate that savolitinib, while used as monotherapy, will predominately be used in combination with other approved targeted drugs. We forecast that savolitinib's first approved indication will be papillary renal cell carcinoma (PRCC), potentially in late 2019 through a breakthrough approval in the US. Our global peak sales expectations are driven by savolitinib's use in multiple different cancers; however, we note the main opportunity is driven by the blockbuster potential in MET+ NSCLC. In our view savolitinib's first approval for NSCLC will likely be in combination with Tagrisso (AZN) for MET+, T790M+/- second-line patients who are resistant to first-generation EGFRm treatment (Iressa/Tarceva). This specific subset of patients has an unmet medical need and, although we forecast 2021 launch, BTD award could lead to earlier approval and launch.

HCM's partnership with AZN remains key to the development of savolitinib and our forecast peak sales. AZN has approved and marketed first- and third-generation EGFR inhibitors in the form of Iressa and Tagrisso. Worldwide, Iressa remains a key first-line therapy for patients with EGFR mutations; however, this will soon be eclipsed by Tagrisso, which is expected to become the standard of care in the US and EU (regulatory packages submitted in both regions). This is on the back of positive data presented at ESMO 2017 ([FLAURA](#)), which demonstrated Tagrisso significantly improved PFS in first-line EGFRm patients when compared with Iressa/Tarceva. Tagrisso has a benefit over first-generation EGFR inhibitors as it targets the exon 20 mutation at position 790 (T790M) in addition to EGFR exon 19 and 21 mutations. First-generation inhibitors Iressa and Tarceva only target EGFR exon 19 and 21 mutations; the majority of acquired resistance to these inhibitors is through T790M, which Tagrisso can target. After T790M acquired resistance, MET is believed to be one of the next major drivers of resistance. HCM and AZN are testing whether combinations of savolitinib and Tagrisso/Iressa will be able to effectively inhibit these multiple cancer proliferation pathways and, in turn, prolong a patient's life.

Following the initial positive proof of concept Phase Ib/II data (presented at WCLC 2017), multiple Phase II/III trials are planned for savolitinib in NSCLC, including:

- A global Phase II/III pivotal study in MET+, T790M-, second-line NSCLC in combination with Tagrisso. The trial will be initiated in 2018, with a potential readout in 2020. The trial will initiate as a three arm Phase II study, powered for both overall response rate (ORR) and progression free survival (PFS). Patients will be randomised to one of two experimental arms or the control arm (chemo-doublet). Patients in both experimental arms will be treated with a combination of Tagrisso and savolitinib, with one arm savolitinib dosed at 300mg and the other at 600mg. Only patients who are refractory to first-generation EGFRm inhibitors (Iressa/Tarceva) will be enrolled into the trial.
- A global Phase III pivotal study in MET+ third-line NSCLC in combination with Tagrisso. AZN will make the decision shortly on whether to proceed subject to the outcome of the mature TATTON B data and preliminary TATTON D results and will engage discussions with regulators. We note

that only patients who are refractory to first- to third-generation EGFRm/T790M inhibitors (Tagrisso) will be enrolled into the trial.

- A China-based Phase III pivotal study in MET+, T790M-, second-line NSCLC in combination with Iressa. Discussions on pivotal studies are ongoing with AZN and HCM. Only patients who are refractory to first-generation EGFRm inhibitors (Iressa/Tarceva) will be enrolled into the trial.

We now assume savolitinib's first launch in NSCLC will be in 2021 as a second-line therapy in combination with Tagrisso in MET+, T790M+/- patients who are refractory to first-generation TKIs. After 2021 we believe potential positive clinical trial data in the other aforementioned trials will lead to further line extensions. We also anticipate HCM and AZN will initiate other trials or expand current trials to incorporate other patient populations. Notably, in our view, this will include second-line MET+, T790M+/- patients who have been treated first line with Tagrisso (following its likely approval in this setting).

In other cancer indications, positive Phase II data presented in PRCC earlier in the year, in addition to the initiation of SAVOIR (a global Phase III trial in PRCC), further validate our underlying assumptions in this indication and, as such, these remain unchanged. Savolitinib is in 14 ongoing clinical trials across PRCC, clear cell renal carcinoma (ccRCC), NSCLC, pulmonary sarcomatoid carcinoma, gastric and prostate cancer. In seven of the trials, savolitinib is being tested in combination with either AZN's durvalumab (PD-L1), AZN's Tagrisso (T790M), AZN's Iressa (EGFR) or docetaxel (chemo).

We note c-Met as a target continues to be validated. The recent release of ASCO 2018 abstracts highlights the range of inhibitors now in development; however, most remain in early development. Most advanced data comes from a Phase II poster presentation testing Merck KGaA's c-Met inhibitor tepotinib in advanced NSCLC patients. Patients enrolled had stage IIIB/IV Met exon14 positive NSCLC without EGFR activating mutations or ALK rearrangements. Patients enrolled had received 0-2 lines of previous therapy and tepotinib was dosed at 500mg a day until disease progression. Final enrolment is expected to be 90 patients. As of the data presented in the [abstract](#), 34 patients had been treated to date with data available for 22. Eleven patients were both MET exon 14 tumour and circulating tumour (ct) DNA positive, 10 were MET exon 14 tumour positive and 1 was ctDNA positive. Of efficacy evaluable patients, 50% (n=9/15) had a confirmed partial response (PR) and another 20% (n=3/15) had stable disease (SD). All responders remained in response at time of data cut-off. 13 patients were eligible for independent review and 46.2% (n=6/13) had a PR with 1 experiencing SD. 13/22 patients had treatment-emergent AEs, with three having grade three AEs. One of these patients experienced a serious AE (interstitial pneumonia).

## **NSCLC: MET patient population proves significant opportunity**

The NSCLC indication could be savolitinib's largest opportunity and it could straddle multiple lines of therapy. HCM's and AZN's NSCLC clinical trial programme is assessing its utility in the first-, second- and third-line setting in certain identifiable patient populations (Exhibit 3).

HCM estimates that the annual incidence of c-Met-driven NSCLC in the US, EU and Japan is around 40,000 to 50,000 patients across all treatment settings. We believe the second-line NSCLC setting in combination with Tagrisso (highlighted in grey in Exhibit 3) is savolitinib's most attractive opportunity: its clinical trial programme is most advanced in the second-line setting and there is potential for BTD given an important unmet medical need in these refractory patient populations.

Recent positive data packages at WCLC (Exhibit 3) highlight the role that savolitinib in combination with EGFR inhibitors can have in addressing MET+ EGFRm NSCLC patients whose disease has progressed following earlier-line treatment with EGFRm inhibitors. We believe the data position savolitinib as a key component of any combination approaches for MET amplified or overexpressed patients.



We view a significant opportunity worldwide in MET+ NSCLC, which we forecast to be predominately driven by combinations with Tagrisso. We calculate the total addressable NSCLC MET population worldwide across first-, second- and third-line treatment at 250,000 patients. However, we note this is based on multiple assumptions, predominately relating to the prevalence of MET as a driver mutation in NSCLC. Based on data so far and the partnership with AZN, we anticipate that, at peak, savolitinib will capture 10% of the global MET+ NSCLC market. Partner AZN now has the dataset to make a decision on savolitinib's global Phase III trials and evaluate the BTD potential. At peak we forecast savolitinib sales in NSCLC of \$2.9bn globally.

In Asia, we anticipate HCM will move forward with a strategy for NSCLC that focuses on combinations with first-generation TKI inhibitors such as AZN's Iressa and Roche's Tarceva, which are now off-patent in China. We forecast that savolitinib will be utilised as both a monotherapy in first-line and in second-line combinations with first-generation EGFR inhibitors (Iressa/Tarceva). While the Chinese healthcare market is quickly catching up with its international peers, we still view it as more fragmented, which could generate reimbursement pressures, although we note HCM has significant experience as a fully integrated domestic player.

Exhibit 3: Savolitinib NSCLC opportunities					
NSCLC line	Mono/combo. MET+,T790M+/-	Eligible NSCLC population	Phase	Clinical trial data	Positioning
First line	Monotherapy  MET+ patients	Of the worldwide 1.7 million new NSCLC patients per year, HCM anticipates 6% are sensitive to a c-Met inhibitor in first-line (either have exon14 skipping or MET gene amplification).	Phase II enrolling.	Savolitinib is being evaluated in an exploratory Phase IIa monotherapy trial in China.	China-focused strategy. Furthest from the market.
Second line	Combination with Tagrisso  MET+ and T790M+/- patients	Patients resistant to first-line treatment with first-generation EGFR inhibitors like Iressa/Tarceva.  HCM anticipates 16% of this second-line patient population are MET+, irrespective of T790M status.	Phase II enrolling.  Pivotal trial initiation in 2018.	Latest data from WCLC 2017. All patients were MET+ confirmed either locally or centrally and all had been previously treated with a first-generation EGFR inhibitor. All patients treated with savolitinib and Tagrisso in combination. Patients who were T790M+ had a 55% partial response (PR) (n=6/11), while a 61% (n=14/23) PR was observed in T790M- patients.	EU and US focused strategy. Expect this setting to be the first launched indication for savolitinib, potentially under BTB.  Phase II/III pivotal trial will be initiated in 2018, with a potential readout in 2020. The trial will be powered for ORR and PFS.
Second line	Combination with Tagrisso  MET+ patients	Patients resistant to first-line treatment with third-generation EGFR inhibitors like Tagrisso. It is currently unknown how many patients will be MET+ following first-line Tagrisso treatment	N/A	We anticipate AZN and HCM will initiate a clinical trial programme once Tagrisso has established itself as the standard of care in first-line for EGFRm NSCLC patients.	EU- and US-focused strategy. Tagrisso is expected to become standard of care in first-line therapy; second-line patients with MET mutations could be a significant opportunity.
Second line	Combination with Iressa  T790M- and MET+ patients	Patients resistant to first-line treatment with first-generation EGFR inhibitors like Iressa/Tarceva.  HCM anticipates 10% of second-line patients have c-Met driven NSCLC without T790 mutation.	Phase II enrolment complete.  Pivotal decision under discussion.	Latest data from WCLC 2017. All patients were MET+ confirmed centrally and had been previously treated with a first-generation EGFR inhibitors. All patients treated with savolitinib and Iressa in combination. Overall, 52% (n=12/23) who were T790M- achieved a PR, whereas in the T790M+ patients only 9% (n=2/23) did. This lower response in T790M+ patients is expected as Iressa is not designed to address T790M+ patients.	China-focused strategy. Could be the second indication savolitinib is launched in globally.  AZN and HCM are in discussions on the NSCLC pivotal study in China.  Pivotal read out potentially in 2021.
Third line	Combination with Tagrisso  MET+ patients	Patients resistant to first-line treatment with third-generation EGFR inhibitors like Tagrisso.  HCM anticipate 30% are c-Met+/T790M+.	Phase II enrolling.  Pivotal decision pending.	Latest data from WCLC 2017. All patients were MET+ confirmed either locally or centrally and all had been previously treated with a third-generation EGFR/T790M inhibitor. All patients treated with savolitinib and Tagrisso in combination. In total, 33% had a confirmed PR (n=10/33).	EU and US focused strategy. Awaiting decision from AZN on pivotal go ahead subject to the outcome of the mature TATTON B data and preliminary TATTON D results and on discussions with regulators.  Pivotal read out potentially in 2021.

Source: Edison Investment Research/ Hutchison China Meditech reports

## TATTON multi-arm trial highlighting savolitinib's potential

In 2014 AZN initiated the [TATTON \(NCT02143466\) study](#), a multi-arm Phase Ib/II study of Tagrisso. The trial aims to test the suitability of an array of therapies with Tagrisso in EGFRm+ NSCLC patients who have progressed following treatment with EGFR TKIs. It has since grown from its initial conception (TATTON A: five arms) to consist of 11 arms across four parts (TATTONS B, C and D). Four of the arms are testing, or have tested, savolitinib in combination with Tagrisso. These are:

- TATTON A: dose-ranging study of savolitinib in combination with Tagrisso. Trial completed.
- TATTON B: savolitinib in combination with Tagrisso at the dose defined in part A. Patients who are T790M negative or positive (T790M +/-) Savolitinib at 600mg oral dose and Tagrisso at 80mg oral dose. Latest data presented at WCLC (Exhibit 4).
- TATTON C: Japan-only study. Savolitinib in combination with Tagrisso. Savolitinib at 400mg oral dose (600mg in other patient populations) and Tagrisso at 80mg oral dose. In the Japanese patients (TATTON A), dose-limiting toxicities were observed at higher doses. Trial ongoing.
- TATTON D: savolitinib in combination with Tagrisso. Savolitinib at 300mg oral dose and Tagrisso at 80mg oral dose. The use of a substantially lower dose of savolitinib (300mg vs 600mg) is to test the effect lower exposure has on the overall safety profile, particularly hepatotoxicity. The effect the 300mg dose has on efficacy vs 600mg will also be recorded. Trial ongoing.

HCM anticipates that during late 2018 or early 2019, the mature TATTON B and preliminary TATTON D data will enable AZN to start discussions with the relevant bodies for second- and third-line regulatory submission.

## PRCC epidemiology study could enable NDA under BTM

The positive data from the Phase II trial in PRCC, along with data from the ongoing MES, could enable a US NDA submission (under the BTM) for the PRCC indication in 2019. The MES is a pooled analysis of over 300 historic patient samples (global) in an effort to determine if c-Met-driven PRCC has worse treatment outcomes/survival than c-Met-independent PRCC. It will give an understanding of how these patients responded to current standards of care such as Pfizer's sunitinib and give clarity on progression-free survival and overall survival (PFS/OS) expected in MET-driven patients. HCM anticipates the data will be available in late 2018 and, in conjunction with the Phase II data, could form part of an accelerated approval under the BTM.

In the Phase II study (data presented as ASCO GU 2017), patients with MET-driven PRCC had a median PFS of 6.2 months (95% confidence interval, CI; 4.1-7.0) vs 1.4 months (95% CI; 1.4-2.7) for MET-independent patients (hazard ratio = 0.33, 95% CI; 0.20-0.52, p<0.0001). There were serious adverse events (AEs) in 23 out of 109 (21%) patients; however, only three of these (four serious AEs in three patients) were considered to be related to treatment. One treatment-related death due to hepatic encephalopathy was reported. Drug discontinuations and dose reductions remained low at 8% (n=9 out of 109) and 13% (n=14 out of 109) respectively. Based on this Phase II PRCC data, savolitinib demonstrates an improved safety profile over other multi-kinase inhibitors in patients with renal cell carcinoma. Prognosis remains poor for patients with advanced PRCC due to limited efficacious treatment options; as such, savolitinib is well placed to capitalise on this unmet need.

Following the positive Phase II study outcome, HCM has initiated [SAVOIR](#), a Phase III 180-patient trial across 50-75 sites globally (US, Europe, Asia and Latin America) that is evaluating savolitinib monotherapy in molecularly selected (via next-generation sequencing) c-Met PRCC patients. The trial is an open-label, randomised study with sunitinib (Sutent) as a comparator arm. Dosing regimens differ between treatments with 600mg of savolitinib (patients who weigh less than 50g will receive 400mg) taken orally with a meal once daily on a continuous basis versus 50mg of sunitinib taken orally with or without food but on a schedule of four weeks on, two weeks off. This dosing regimen is

driven by sunitinib's relatively toxic profile, which means an off-treatment period is required. Initial data are expected in 2020.

## **c-Met trials ongoing in ccRCC, lung, gastric and prostate cancer**

HCM is exploring savolitinib's potential in an array of cancers as data so far indicate c-Met abnormalities can often be a key driver of the disease. In addition to PRCC, HCM has ongoing trials testing savolitinib's suitability in ccRCC. A [Phase II \(CALYPSO\)](#) combination study with AZN's durvalumab (PD-L1 inhibitor) is ongoing in both PRCC and ccRCC. It is split into three parts, with the second stage ongoing. The first stage found the optimal dose of durvalumab (Imfinzi) and savolitinib in PRCC patients, in the second stage patients with PRCC are being treated at the optimal dose, while ccRCC patients are randomised into one of four treatment arms. These include the two compounds in combination and as monotherapies in addition to a combination arm of durvalumab and tremelimumab (CTLA-4 inhibitor). In the final stage of the trial, patients will be tested before treatment for biomarkers then enrolled into the appropriate arm of durvalumab, savolitinib or durvalumab and tremelimumab. Initial data are expected in late 2018.

In lung cancer, HCM has an ongoing [Phase II trial](#) in lung sarcomatoid carcinoma, a rare type of the disease with no approved targeted therapies. The trial is using savolitinib in first-line c-Met-driven Chinese patients. The trial aims to enrol patients with a MET exon 14 mutation who are unwilling or unable to receive chemotherapy, although patients who have also failed prior systemic therapies will also be enrolled.

Outside of lung and kidney cancer, HCM is focused on gastric cancer in Asia, where incidence of the disease is high. Each year there are approximately 450,000 new cases in China, of which 10% have MET amplification. An umbrella trial (VIKTORY), run by Samsung Medical Centre, is ongoing. The study is molecularly screening patients and consequently allocating them to a relevant treatment arm. As of the most recent update at ASCO 2017, 432 patients had been enrolled and screened for genomic profiling. Of these, 124 have been treated on one of the treatment arms. In total, 23 of the 432 patients presented c-Met aberrations (5.3%), 19 were enrolled into a treatment arm with a combination of savolitinib and docetaxel, with the remaining four patients enrolled for treatment with savolitinib as a monotherapy. Of the four patients who were treated as a monotherapy (Phase Ib), patients were c-Met gene amplified and preliminary efficacy has been observed to date. In the combination arm (Phase Ib) with docetaxel, patients were c-Met overexpressed or c-Met gene amplified; dose-finding studies are ongoing.

## **Savolitinib: Peak sales potential of \$5.9bn across current indications**

We forecast global peak sales for savolitinib of \$5.9bn (PRCC, CRCC, NSCLC, pulmonary sarcomatoid and gastric cancer indications). Our increased forecasts are driven by the increasing peak penetration in NSCLC and probability of success. Additionally, we have reassessed our expected launch dates (and thus peak year of sales) and have pushed back launch years across indications (Exhibit 4), notably with the first indication launch (in PRCC) now forecast for 2019 (previously 2018). Note, we forecast peak sales in China as seven to eight years from launch, and five years from launch in the rest of the world.

**Exhibit 4: Savolitinib peak sales forecasts**

Product	Indication	Launch year/ peak sales China	Launch year/ peak sales RoW	Assumptions
Savolitinib	PRCC	2020/2027 \$64.2m	2021/2025 \$267.1m	Global 2015 new cases (50,000), China 2015 new cases (7,800). MET amplification 40-70%, therefore assume higher penetration rates. China penetration 10%, \$5,000 per month, 12-month treatment duration. RoW penetration 4.5%, \$10,000 per month, 12-month treatment duration.
	Clear cell renal carcinoma	2022/2028 \$169m	2022/2027 \$987m	Global 2015 new cases (270,000), China 2015 new cases (54,000) MET over-expression 79%. China penetration 4%, \$5,000 per month, 12-month treatment duration. RoW penetration 3%, \$10,000 per month, 12-month treatment duration.
	NSCLC	2021/2027 \$387m	2021/2027 \$2.5bn	Global new cases (1,690,000), China new cases (623,000). MET mutations 6% in first-line NSCLC, 16% MET mutations in second-line EGFR treated (Iressa) patients, while 30% in third line following third-generation EGFR (Tagrisso) treatment. China penetration 10% MET+ market across lines of treatment, \$5,000 per month, 12-month treatment duration. RoW penetration 10% MET+ market across lines of treatment, \$10,000 per month, 12-month treatment duration.
	Gastric cancer	2022/2029 \$326m	2023/2027 \$750m	Global new cases (1,034,000), China new cases (454,000) MET amplification 10%. China penetration 1%, \$5,000 per month, 12-month treatment duration. RoW penetration 0.8%, \$10,000 per month, 12-month treatment duration.
	Pulmonary sarcomatoid carcinoma		2021/2028 \$476m Global	Global new cases (34,000) Global penetration 17%, \$5,000 per month, 12-month treatment duration.
	Deal economics			\$140m in initial upfront and milestones from AZN royalty rate 30% on China, subject to approval in the PRCC indication, HCM will receive tiered royalty rates of 14-18% across all indications. After total aggregate sales of savolitinib have reached \$5bn, the royalty will reduce over a two-year period, to an ongoing royalty rate of 10.5% to 14.5%.

Source: Edison Investment Research. Note: FX rate \$1.35/£. Note we forecast peak sales in China as seven to eight years from launch, and five years from launch for RoW.

Exhibit 4 details our savolitinib's peak sales potential by indication, incident rates and penetration assumptions. We assume pricing of \$10,000 per month in the US and ROW ex-China with a treatment course duration of 12 months, with China priced at a 50% discount. We believe this is conservative given that the average US retail price is \$15,942.79 per month for AZN's Tagrisso (40mg dose), a third-generation TKI (source: Goodrx.com). Our model assumes a 30% royalty on China sales and 14-18% tiered royalty on ROW sales payable to HCM from AZN and up to \$100m more in milestone payments as per deal terms. We have not included milestone payments on further sales after initial launch, which would significantly enhance our valuation. We note that under the terms of the agreement with AZN, the royalty rate is expected to step down to 10.5-15.5% upon reaching aggregate savolitinib sales of \$5bn.

We have increased our peak penetration rates in NSCLC. Data from HCM to date demonstrate that MET mutations after second-line Tagrisso treatment occur in approximately 30% of patients, a higher percentage than patients who received Iressa or Tarceva in the first line (c 16%).

For our modelling, we forecast the total eligible MET population as a combination of:

- c 100,000 first-line MET+ NSCLC patients globally, MET-driven patients represent 6% of the total NSCLC market ;
- c 80,000 second-line MET+ NSCLC patients globally, 30% of NSCLC patients receive first-line EGFR treatment, after which 16% of this population is MET-driven; and
- c 70,000 third-line MET+ NSCLC patients globally, 45% of second-line patients are treated with Tagrisso of which 30% go on to be MET+.

We note that the number of MET-driven patients remains a key sensitivity for our analysis. As the c-Met market remains in its infancy, our assumptions are based on figures from HCM but sense checked against current literature. Materially different MET-driven patients in any line of treatment could have a significant effect on our valuation. Literature has highlighted a range of MET+ rates in NSCLC ranging from 4% in surgically resected patients, 20% in EGFRm pre-treated to 51% in mixed wild-type and mutated NSCLC patients. Additionally, changes to mutation levels in the presence of other driver mutations further complicate the ability to define exact numbers (ALK+ patients have increased MET receptor expression of up to 66%). Differences in trial design, testing methods and

MET mutation definitions (eg the amount of gene copy numbers and receptor amplifications) will all affect the levels reported. We await future data packages to give further clarity on this matter.

As Tagrisso moves to first-line treatment ([MAA submitted to the EMA](#) and [sNDA submitted to the US FDA](#)), MET+ patient numbers may increase in the second line above what is seen when patients are treated with first-generation EGFR inhibitors (Iressa/Tarceva). However, uncertainty remains on this particular patient segmentation, so for our second-line modelling assumptions we use MET status (c 16%) following Iressa/Tarceva. In third-line patients we use a 30% MET status based on the Tagrisso data so far.

Based on the positive data at WCLC, we have increased our peak penetration rate globally in total MET NSCLC patients to 10% of the market (across all lines of treatment), ~25,000 patients. In China, we anticipate that at peak savolitinib will be able to capture 10% of the total MET population (across all lines of treatment). While there is limited insurance coverage in China and a fragmented healthcare system (dependent on private payers), we believe this penetration rate is reasonable due to HCM's expertise in the market.

We have also increased our probability of success to 75% (from 50%) driven by this data and, in our view, an impending Phase III NSCLC trial initiation. We note an increased interest over the last 12 months from many multinational pharmaceutical companies has led to an increase in the development of c-Met inhibitors in NSCLC, which could limit savolitinib's peak sales. However, in our view savolitinib demonstrates best-in-class characteristics along with a first-mover advantage that should enable savolitinib to capture significant market share in NSCLC.

We note significant sensitivities around our assumptions, particularly within NSCLC due to the large contribution it now makes to our valuation. Limited efficacy in Phase III trials, lower levels of MET amplification than expected, increased competition and changes in treatment dynamics could all materially affect our valuation.

The growing market awareness of savolitinib's blockbuster potential (across multiple treatable c-Met-driven cancers) is generating interest from global pharmaceutical companies. In our view, savolitinib's closest competitors are small molecule selective inhibitors capmatinib (INC280) from Novartis and tepotinib (MSC2156119J) from Merck. While we view developers of other selective c-Met inhibitors as main competitors, fast-moving treatment paradigms mean many indirect competitors remain. We view immune checkpoint inhibitor (ICI) combinations as the main threat to the success of c-Met treatments although this could be offset by the success of the ongoing savolitinib and ICI combinations. We anticipate that first-line cancer treatment will be driven by relevant driver mutations like EGFRm, while ICIs will likely be saved for patients with no treatable mutations. However, multiple dynamics are at play and a simplified view of first- or second-line treatment (eg chemotherapy as standard across first-line patients) may no longer hold and will instead be determined on a case-by-case basis.

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## **Fruquintinib FRESCO ready for market launch in 2018**

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Fruquintinib is an oral small molecule that is a highly selective VEGFR1, VEGFR2 and VEGFR3 inhibitor. HCM is developing fruquintinib outside China (although Lilly has the option to opt in) and in partnership with Lilly in China. The NDA for fruquintinib for third-line CRC was submitted to the CFDA in June 2017 and we anticipate fruquintinib approval and launch in China in Q418. On approval, HCM's Suzhou production facility will be used to produce fruquintinib for commercial supply; it is now entering the CFDA pre-approval inspection and GMP certification stage as part of the NDA process.

The first-generation VEGFR inhibitors revolutionised the treatment of cancer (Avastin peak sales of CHF6.8bn in 2016) by targeting the growth of blood vasculature that is essential for tumour growth (anti-angiogenesis). There remains a need for a small molecule (oral) VEGFR inhibitor that positively impacts PFS and OS with a more tolerable side-effect profile than intravenously administered biologic

agents such as Avastin. Fruquintinib's lower rate of adverse events leading to VEGFR discontinuation (4% vs 41% on Avastin) and hypertension (4% vs 60% on Avastin, note not head-to-head data) should enable it to be given in combination with other small molecule TKIs.

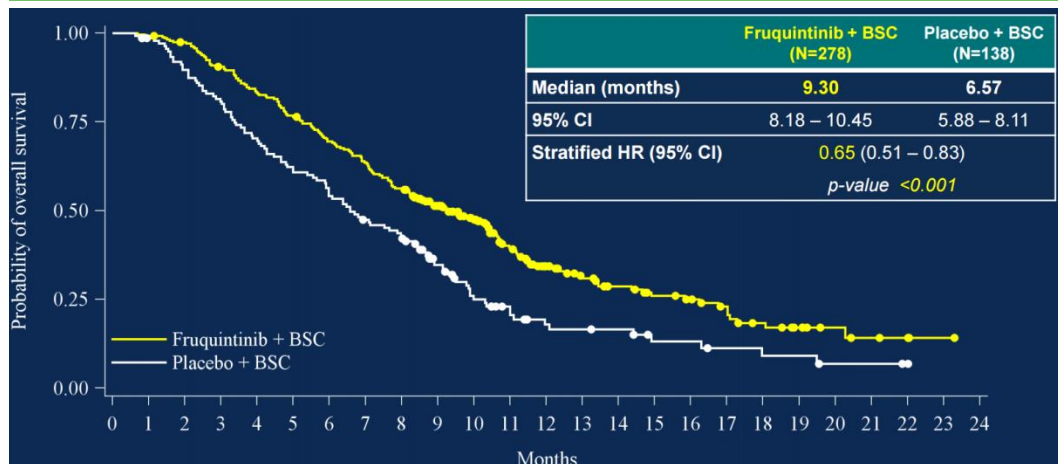
Fruquintinib's most advanced indications are in CRC (third-line) and NSCLC (third-line) in China. Following the presentation of multiple fruquintinib data sets throughout 2017 (bullet pointed below) we update our fruquintinib assumptions.

- We now assume fruquintinib's use in combinations could drive its utilisation in earlier lines of therapy. This compares with our original expectations, which focused mainly on refractory or third-line use. As such, our NSCLC peak penetration rates for China are higher at 1.5% (previously 1.0%). We maintain 1% penetration globally (ex-China). Positive FRESCO Phase III data on fruquintinib in third-line CRC at ASCO 2017 (statistically meaningful improvement in both OS and PFS and a manageable side-effect profile) triggered the China NDA submission (third-line CRC) in June 2017; we expect approval and launch in China in Q418.
- Positive preliminary data presented at WCLC 2017 from an ongoing Phase II trial testing fruquintinib (VEGFR inhibitor) in combination with Iressa in first-line EGFR-mutant NSCLC support this unique VEGFR inhibitor's role in combination therapy. While a small number of patients were observed, the impressive efficacy supports our increased sales expectations for fruquintinib as we anticipate earlier use in NSCLC.
- Trials ongoing include two Phase II trials in third-line NSCLC and second-line gastric cancer, in addition to a pivotal China Phase III trial (FALUCA) in third-line NSCLC (monotherapy) (top-line data expected in Q418). HCM has also initiated a pivotal Phase III trial in China evaluating fruquintinib in combination with Taxol (chemotherapy) in second-line gastric cancer.
- In the US, a Phase I bridging study is enrolling patients in the dose escalation component of the study. This should determine the dose required to take fruquintinib into US Phase II/III studies across its differing indications in preparation for a US NDA submission.

## **FRESCO data give first Phase III confirmation of HCM strategy**

FRESCO data (third-line CRC) underpin the hypothesis that fruquintinib's safety and efficacy profile could enable it to be positioned as best-in-class in China. Its profile internationally will be determined by global Phase III trials (data from FRESCO bode well) as we believe the global clinical trials will focus on more proprietary combination studies. CRC is believed to be one of the five most common cancers in both Chinese men and women, with an estimated [191,000 deaths in China in 2015](#) (incidence of 376,000 in 2015). At ASCO 2017 full data were presented from [FRESCO](#), the China-based pivotal Phase III trial in third-line CRC patients. Both OS and PFS (Exhibit 5) demonstrated statistical significance over placebo, a notable clinical achievement when considering the difficult patient population in which fruquintinib was tested. Key points include a median OS of 9.30 months in the fruquintinib group (95% CI, 8.18-10.45) vs 6.57 months in the placebo group (95% CI 5.88-8.11) ( $p < 0.001$ ) and a median PFS was 3.71 months (95% CI 3.65-4.63) vs 1.84 (95% CI 1.81-1.84) for placebo.

**Exhibit 5: FRESKO overall survival (third-line CRC)**



Source: Hutchison China MediTech

Safety will be a key differentiator for fruquintinib as it looks to position itself in the Chinese market as a best-in-class product. Dose interruptions, a key indicator of tolerability, were 35.3% (n=98) in the fruquintinib arm and 10.2% (n=14) in the placebo arm, while treatment discontinuation was 15.1% (n=42) and 5.8% (n=8) in each arm respectively. An in-depth analysis of the FRESKO data can be found in our note, [ASCO data set up fruquintinib for China launch](#).

## Opportunities in NSCLC as combinations demonstrate promise

Fruquintinib is in two ongoing trials in NSCLC, as a monotherapy (Phase III) in third-line patients and in combination (Phase II) with Iressa in first-line patients. While there are no planned combinations of fruquintinib with Tagrisso and/or savolitinib in NSCLC, we believe any combinations could be synergistic. Data presented at WCLC 2017 from an ongoing Phase II trial testing fruquintinib (VEGFR inhibitor) in combination with Iressa in EGFR-mutant NSCLC patients support this unique VEGFR inhibitor's role in combination therapy, albeit in a small patient population. The trial tested fruquintinib at 4mg or 5mg once daily for three weeks on, one week off in combination with 250mg of Iressa once daily. In total, 17 patients were eligible for efficacy evaluation, of which 13 (four PRs not confirmed as of data cut-off) (76.5%) had a partial response and four had stable disease (23.5%). No patients as of data cut-off had progressive disease and the median time to response was 56 days. A 4mg dose of fruquintinib was determined to be most suitable for further investigation as liver enzyme elevation was observed at 5mg. Overall, eight out of 26 (30.8%) patients reported grade 3-4 AEs, five of which were increases in alanine transaminase as a result of damage to the liver.

FALUCA, the Phase III registration trial in China, was initiated in December 2015 for third-line treatment in NSCLC, following a positive Phase II POC trial that reached the primary end point of PFS with no unexpected safety issues. FALUCA is a double-blind, placebo-controlled Phase III (n=527) evaluating fruquintinib 5mg once a day plus best supportive care in four-week treatment cycles (three weeks on drug, one week off). We expect HCM/Lilly to submit an NDA for fruquintinib in NSCLC (third line) to the CFDA in late 2018/early 2019. We model a potential launch in this indication in 2020. The speed of any approval is less clear than with the US FDA, but we expect it to take around 12 months.

## Gastric cancer FRUTIGA Phase III initiated (second line with Taxol)

HCM has initiated a pivotal Phase III (FRUTIGA) combination trial (second line) evaluating fruquintinib and established chemotherapy agent Taxol (paclitaxel) for the treatment of advanced gastric cancer patients (n>500) who have progressed after first-line standard chemotherapy (5-

fluorouracil and platinum doublets); top-line data are expected in 2020. Primary efficacy endpoint for FRUTIGA is OS, secondary endpoints include PFS, overall response rate (ORR) and disease control rate (DCR). We note that biomarkers related to the anti-tumour activity of fruquintinib will also be explored. At ASCO GI 2017, HCM presented data from the open-label, Phase Ib dose-finding/expansion study of fruquintinib in combination with paclitaxel in second-line advanced gastric cancer (n=32); 28 patients were evaluable for efficacy (tumour response) of which 10 achieved confirmed partial response (ORR=35.7%), and nine experienced stable disease for at least eight weeks (DCR=67.9%). The National Central Cancer Registry of China reports an incidence of 679,000 gastric cancer cases and 498,000 gastric cancer deaths in China in 2015. Most Chinese gastric cancer patients receive chemotherapy and few targeted therapies are approved, with limited salvage treatments in third line and above.

## Fruquintinib: Peak sales potential of \$2.2bn across all indications

Exhibit 6 details our peak sales forecasts and assumptions by indication. We forecast global peak sales for fruquintinib of \$2.2bn across all indications under investigation (CRC, NSCLC and gastric cancer). Our underlying expectations have changed; our upwardly revised NSCLC numbers take into consideration fruquintinib use in first- and second-line settings as combination therapy versus our main prior assumption of use in the main as third-line monotherapy. We therefore increase our penetration rates to 1.5% of the Chinese market (previously 1% and 1.5%). Our model assumes a tiered 15-20% royalty on China sales payable from Lilly. Additionally, we have increased our monthly pricing assumption to \$3,500 from \$2,500, we note competitor product apatinib (Jiangsu HengRui Medicine) is priced at \$2,870 per month. We believe fruquintinib to be a superior product given it doesn't inhibit the CYP450 (where as apatinib does).

Previously we modelled 11% RoW royalty on sales payable to HCM from Lilly based on the assumption that Lilly would exercise its option on the global development of fruquintinib. However, we now forecast that these rights revert back to HCM and it will fund development and commercial costs worldwide. In the US, a Phase I bridging study in Caucasian patients was initiated by HCM in December 2017. This should determine the dose required to take fruquintinib into US Phase II/III studies across its differing indications in preparation for a US NDA submission. We expect fruquintinib to enter US Phase II/III trials and anticipate additional indications after the bridging study to be determined by a range of factors including combination potential and achievable market.

We note NPV contribution for sales outside China has increased greatly due to higher economic value retained (despite the need for R&D, and S&M expenses) by not partnering the asset globally.

**Exhibit 6: Fruquintinib peak sales forecasts**

Product	Indication	Launch year/ peak sales China	Launch year/ peak sales ROW	Assumptions
Fruquintinib	CRC	2018/2024 \$149m	2022/2026 \$565m	Global new cases (1,477,000), China new cases (283,000). China penetration 1.0%, \$3,500 per month, 12-month treatment duration. RoW penetration 0.7%, \$5,000 per month, 12-month treatment duration.
	NSCLC	2020/2026 \$334m	2021/2026 \$721m	Global new cases (1,690,000), China new cases (623,000), China penetration 1.5%, \$3,500 per month, 12-month treatment duration. RoW penetration 1.0%, \$5,000 per month, 12-month treatment duration.
	Gastric cancer	2020/2027 \$292m	2022/2027 \$392m	Global new cases (1,034,000), China new cases (454,000). China penetration 2%, \$3,500 per month, 12-month treatment duration. RoW penetration 1%, \$5,000 per month, 12-month treatment duration.
Deal economics				Deal economics: \$86.5m in upfront and milestones from Lilly, royalty rate 15-20% on China. Lilly is funding majority of development costs and all commercial costs in China. HCM to fund development and commercial costs worldwide.

Source: Edison Investment Research. Note: FX rate \$1.35/£. Note we forecast peak sales in China as seven to eight years from launch, and five years from launch for RoW.



## Other late-stage assets progressing as expected

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### Sulfatinib enrolling pivotal Phase III trials

Sulfatinib is an oral angio-immunokinase inhibitor that targets VEGF1, 2 and 3, FGFR1 and colony stimulating factor 1 receptor (CSF-1R) kinases. CSF-1R is a cell-surface protein that acts as the receptor for the cytokine CSF1, which controls macrophage (a type of white blood cell) function. [Inhibition of CSF-1R](#) limits the production of pro-tumour macrophages which, among other functions, is believed to aid in angiogenesis, tumour cell invasion and evasion of the immune system. This mechanism of action could further differentiate it from other VEGFR inhibitors. HCM presented positive preliminary data in both pancreatic (ORR 17.1% based on confirmed PRs; DCR 90.2% and median PFS 19.4 months) and non-pancreatic (ORR 15.0% based on confirmed PRs; DCR 92.5% and median PFS 13.4 months) neuro endocrine tumours (NETs) at the ENETS conference in early 2017. Phase III studies (SANET-p in pancreatic NETs and SANET-ep in non-pancreatic NETs) have started enrolling in China. Additionally, a Phase II POC study in biliary tract cancers has also initiated in China.

### Epitinib moving to Phase III trials in NSCLC with brain metastases

Epitinib is a selective EGFR TKI designed for optimal brain penetration to target brain metastases (BM) associated with EGFR mutation-positive solid tumours. We have increased our epitinib probability of success in NSCLC with brain metastasis to 75% (from 30%) based on the soon-to-initiate China Phase III clinical trial, once the Phase III dose regimen has been decoded. A Phase Ib/II study in glioblastoma (high EGFR gene amplification) initiated in March 2018.

## Second wave of candidates moving up

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Longevity for R&D-driven biopharmaceutical companies is dependent on having a pipeline of innovative assets that span development phases. HCM's second wave of innovation candidates (theliatinib, HMPL-523, HMPL-689 and HMPL-453) are in dose-escalation Phase I and/or are poised to enter Phase Ib/II clinical development (POC clinical trials) for oncology and immunology indications. HCM hopes to generate enough data in the next 12-18 months to sufficiently demonstrate POC for these compounds. We note that HMPL-689 and HMPL-453 contribute zero to our valuation (we typically include Phase II assets for HCM) and as such we would anticipate progress to POC to increase our risk-adjusted valuation of the company. The next candidate to progress into Phase II is likely to be HCM's SYK inhibitor HMPL-523, potentially for immunology indications such as rheumatoid arthritis and also in haematological cancers.

The 2017 progress for the second wave of candidates is listed below:

- HMPL-523 (SYK inhibitor for oncology and immunology indications): HCM has submitted an IND for autoimmune diseases to the US FDA. Pending the submission of additional data (relating to a metabolite of the product) requested by the US FDA, the Phase II POC in an immunology indication (likely rheumatoid arthritis) could initiate in late 2018/early 2019. The RP2D has been established in Phase I dose-escalation studies in Australia and China in patients with haematological malignancies. HCM is increasing the number of trial sites to support the Phase Ib/II expansion in a range of indolent NHL (non-Hodgkin's lymphoma) sub-types.
- HMPL-689 (PI3K delta inhibitor for haematological cancer): China IND has been accepted and a dose-escalation study in haematological cancer patients was initiated in August 2017.
- Theliatinib (EGFR wild-type inhibitor for solid tumours): Phase Ib POC expansion monotherapy study in oesophageal cancers (EGFR overexpression or gene amplification) in China initiated.

- HMPL-453 (FGFR1, 2, 3 inhibitor): Phase 1 dose escalation studies initiated in Australia and China in patients with solid tumours.

## Own commercial strategy to enhance returns

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In the medium term, we expect HCM to capitalise on its substantial China-based commercial presence by launching its wholly owned assets into the domestic market through its CP division. During the last two years, HCM has increased its footprint in China and its extensive commercial network now consists of a 3,300-person sales team; including 2,300 medical reps for prescription drugs, 1,000 OTC sales reps covering more than 300 cities and towns detailing to c 98,000 doctors across c 22,500 hospitals. Importantly, this established commercial network will be invaluable in launching the innovative product portfolio in China. Whilst we anticipate an increase in costs relating to launch and support of these products and the need to hire specialist reps, we note HCM has much experience in operating in its domestic market. Additionally, it has garnered knowledge in the regulatory aspect of bringing new drugs to market through working alongside partners AZN and Lilly.

In terms of international commercial opportunity, a key assumption in our initiation note 'Stellar Evolution' published May 2016 was that HCM would seek partners for each wholly owned asset around phase II development status in return for 30% royalty on sales plus milestones. However during the last two years HCM has grown significantly; its broad product pipeline has matured with proof of concept clinical data on many of its assets, its financial strength has increased through its initial and follow-on public offerings on Nasdaq (raising net \$411.5m), and the ongoing substantial cash generation from its China commercial platform business. HCM is at an inflection point in its commercial strategy and we forecast that it will retain the non-China rights to Fruquintinib. Whilst this gives HCM the responsibility for its drug development program outside China (and thus the associated costs); it also means that HCM can start to initiate its global commercial strategy based initially on fruquintinib but with the view to leverage the late stage oncology portfolio given multiple potential drug approvals in 2020/21. However, we highlight failure of one or more assets at either Phase III or failure to be approved would impede on our operational leverage expectations. We anticipate significant operational leverage in the medium term from the two platforms; this would serve as a major source of uplift in economic returns.

## Commercial Platform highly cash generative

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CP refers to HCM's China-based business and is its primary profit- and cash-generative division. This business consists of numerous joint ventures established with well-known Chinese healthcare company peers (Shanghai Pharmaceuticals, Sinopharm group and Guangzhou Baiyunshan). Over the past 18 years, HCM has built a broad consumer health (mainly OTC) and prescription-only drug (including traditional Chinese medicine) fully integrated, manufacturing, marketing and distribution network that reaches across China.

Full-year 2017 results published in March 2018 highlighted robust growth within the CP division. Total consolidated sales reported at \$205.2 (+13%, 2016 \$180.9m). Total sales of non-consolidated JVs increased by 6% to \$472.0m. Total consolidated net income attributable to HCM increased by 25% to \$37.5m (adjusted non-GAAP basis excluding one-time gains of R&D subsidiaries and property compensation). The CP is subdivided into prescription drugs and consumer health.

Prescription drugs consist of two pharmaceutical JVs, FY17 consolidated sales of \$166.4m (+11%), total non-consolidated JV sales +10% to \$244.6m, total consolidated net income attributable to HCM +28% to \$26.5m (adjusted non-GAAP basis excluding one-time gains).

- Shanghai Hutchison Pharmaceuticals (SHPL) is a 50/50 joint venture with Shanghai Pharmaceuticals and focuses on prescription traditional Chinese medicines. SHPL holds a large portfolio of registered drug licences, including its own and third party. SHPL's main product is SXBX pill (She Xiang Bao Xin Wan) for coronary heart disease. Sales grew 7% to \$209.2m in 2017 vs +23% H117 was affected by a price increase (implemented late 2016 and early 2017); however, pricing and volumes benefited sales in H217 and HCM reported a material improvement in margins in the product. SXBX has a 15% market share of China's \$2bn coronary disease drug market. SXBX is patent protected in China through to 2029; growth is aided by its inclusion on the Essential Medicines List (all Chinese state-owned healthcare institutions are required to carry the drug) and is fully reimbursed in all provinces in China. SXBX will continue to benefit from rising rates of obesity and an aging population predisposing factors for coronary artery disease. The SHPL JV is a large-scale commercial and manufacturing operation, its new GMP certified factory (located 40km outside of Shanghai) has tripled capacity, positioning the group for long-term growth.
- Hutchison Sinopharm, a third-party prescription logistics and distribution service, reported sales of \$166.4m in 2017 (+11%). Growth drivers include the third-party drug distribution of Seroquel (an atypical anti-psychotic drug). Hutchison Sinopharm is the exclusive marketing agent for AZN's Seroquel, which holds a 5.6% market share in China's \$0.9bn atypical anti-psychotic drug market. Reported 2017 sales were affected by the new China two-invoice system (TIS) that came into effect in October 2017. Hutchison Sinopharm can no longer book gross sales of Seroquel in its top-line revenues and has shifted to a fee-for-service model; there is no impact on a profitability basis. As a result of the TIS, HCM is guiding Hutchison Sinopharm sales of \$75-85m for 2018.

Consumer Health consists of two wholly-owned subsidiaries and two JVs. Reported combined non-consolidated sales were \$266.2m in 2017 (\$255.1m in 2016) and consolidated net income attributable to HCM increased by 20% to \$11m.

- Hutchison Baiyunshan (HBYS) is a 50/50 joint venture with Guangzhou Baiyunshan, principally focused on OTC TCM. HBYS has 189 registered TCM products. In September 2017, HBYS divested its 60% shareholding in Guanbao, a low-margin, third-party OTC business with no strategic value to the HCM group. HBYS reported sales for Guanbao in 2017 of \$38.6m. HCM's 2018 guidance for the group included one-time property gains (\$0-20m) from the potential sale of HBYS's vacant plot in Guangzhou; the timing of this is subject to Guangzhou government policy.

We expect the CP to continue to post double-digit sales and net income growth in the near term; however, we note that the impact of the TIS and Guanbao divestiture will lead to lower reported top-line sales in 2018. Net profit growth, however, is expected to have minimum impact. HCM has issued guidance for consolidated sales of \$115-125m in 2018 and net income of \$41-63m. We forecast consolidated net income of \$41.5m for 2018 in this division.

## Sensitivities

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HCM is subject to the usual biotech and drug development risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. The key sensitivities for HCM relate to crystallising value from the mid- to late-stage pipeline, in particular savolitinib, fruquintinib, sulfatinib and epitinib; these products contribute to the majority of our valuation. We note that as a result of our upgrades fruquintinib, and savolitinib now represent 37% and 25% respectively of our valuation of the company. Economic uncertainties will always exist in China, although we believe government measures to open up the private healthcare insurance market to international players on top of extensive (although less broad) universal state

coverage should help to address these concerns. Furthermore, uptake of the more expensive innovative cancer drugs is likely to be skewed to the growing and increasingly affluent middle-class population.

## Valuation

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We have significantly increased our SOTP valuation (Exhibit 7) to \$6.4bn or £71.0/share (vs \$2.7bn, or £36.1/share in June 2017). The major sources of uplift are 1. Increased peak sales forecasts for savolitinib and fruquintinib in NSCLC; these assets are key valuation drivers, given their potential blockbuster status and timeframe to market 2. Changing the economic terms for the wholly owned assets (fruquintinib ex-China, and globally for sulfatinib, epitinib, theliatinib, HMPL-523) from our prior flat 30% royalty rate on sales assumption to full value retained by HCM (we decrease peak sales for these assets ex China and now reflect product operating expenses relating to sales and marketing and infrastructure costs) and 3. We introduce a terminal value for the first time to our valuation of HCM to reflect the maturity of the company and depth of the rest of the pipeline.

We value the Innovation Platform (IP) at \$4,702.6m and placing Commercial Platform's (CP's) 2018e share of net profit on a 20.4x rating gives \$848.2m (945p/share). We have updated our model for FY17 results, rolled forward our DCF and updated our probabilities of success for assets that have progressed and have pushed back some launch dates by 1-2 years. Adding in December 2017 net cash results in a value of \$6.4bn or £70.1/share. We use 10% discount rate and 1% growth rate in calculation of terminal value of \$491.8m which represents 8% of our total valuation of the company. 10% is our standard discount rate assumption for companies with approved products and minimal development risk.

With the CP, we look at the earnings multiples of peers quoted on the Chinese stock exchanges. Using a 20.4x multiple (in line with the sector (non-weighted) average for comparable domestic Chinese companies) on the 2018 forecast net attributable profit of \$41.5m for the CP unit results in a valuation of \$848.2m.

Exhibit 7 details the breakdown of contribution from products by indication to our risk-adjusted NPV. However, we have included the non-risk adjusted NPV (shaded in grey) to illustrate the potential value of the pipeline should all projects in our forecasts succeed. Projects in preclinical development or early Phase I are not yet included in our valuation.

**Exhibit 7: HCM valuation**

Product	Indication	Launch	Peak sales (\$m)	Value (\$m)	Probability	rNPV (\$m)	rNPV/share (\$/share)	rNPV per share (£)	rNPV/ADS (\$/ADS)	NPV* per share £
Savolitinib (AZD6094/volitinib)	Papillary renal cell carcinoma	2020 (China)	\$64m (China)	203.5	75%	152.0	2.3	1.7	1.1	2.3
		2021 (ROW)	\$267m (ROW)							
	Clear cell carcinoma	2022 (China)	\$169m (China)	310.3	35%	107.0	1.6	1.2	0.8	3.5
		2022 (ROW)	\$987m (ROW)							
	NSCLC	2021 (China)	\$387m (China)	815.3	75%	611.4	9.2	6.8	4.6	9.1
		2021 (ROW)	\$2.5bn (ROW)							
	Gastric Ca	2022 (China)	\$326m (China)	336.8	35%	115.4	1.7	1.3	0.9	3.8
		2023 (ROW)	\$750m (ROW)							
	Pulmonary sarcomatoid ca	2021 (Global))	\$476m (Global)	359.6	50%	178.8	2.7	2.0	1.3	4.0
Fruquintinib	CRC	2018 (China)	\$149m (China)	772.3	90%	695.1	10.4	7.7	5.2	8.6
		2022 (ROW)	\$565m (ROW)							
	NSCLC	2020 (China)	\$334m (China)	1,090.4	75%	817.8	12.3	9.1	6.1	12.1
		2021 (ROW)	\$721m (ROW)							
	Gastric Ca	2020 (China)	\$292m (China)	713.1	75%	534.8	8.0	6.0	4.0	7.9
		2022 (ROW)	\$392m (ROW)							
Sulfatinib	NET	2021 (China)	\$79m (China)	841.6	75%	631.2	9.5	7.0	4.7	9.4
		2021 (ROW)	\$454m (ROW)							
	Thyroid ca	2021 (China)	\$72m (China)	279.3	50%	139.7	2.1	1.6	1.0	3.1
		2022 (ROW)	\$212m (ROW)							
	Biliary Tract	2023 (China)	\$190m (China)	344.0	50%	165.5	2.5	1.8	1.2	3.8
		2023 (ROW)	\$137m (ROW)							
Epitinib	NSCLC	2021 (China)	\$198m (China)	520.7	75%	390.5	5.9	4.3	2.9	5.8
		2022 (ROW)	\$212m (ROW)							
Theliatinib	Oesophageal ca	2022 (China)	\$328m (China)	618.1	10%	61.8	0.9	0.7	0.5	6.9
		2022 (ROW)	\$129m (ROW)							
HMPL-523	RA	2023 (WW)	\$1.6bn (Global)	801.5	10%	80.1	1.2	0.9	0.6	8.9
			Haematological cancers	2023 (WW)	\$95m (China)	121.5	30%	21.5	0.3	0.2
<b>Valuation of IP only</b>				<b>\$8,128.0</b>		<b>\$4,702.6</b>	<b>\$70.70</b>	<b>£52.37</b>	<b>\$35.35</b>	<b>£90.52</b>
CP				848.2	100%	848.2	12.75	9.45	6.38	9.4
<b>Net cash December 2017</b>				<b>328.3</b>	<b>100%</b>	<b>328.3</b>	<b>4.9</b>	<b>3.66</b>	<b>2.47</b>	<b>3.7</b>
Terminal value				491.8	100%	491.8	7.4	5.48	3.70	5.5
<b>Valuation</b>				<b>\$9,796.3</b>		<b>\$6,370.9</b>	<b>\$95.8</b>	<b>£70.95</b>	<b>\$47.89</b>	<b>£109.09</b>

Source: Edison Investment Research. Note: \*Non-risk adjusted NPV per share assumes 100% probability of success. \*\*Probability reflects likely filing with Phase II data for BT. FX rate \$1.35/£. Number of shares outstanding 66.52m. Ca. = cancer

The main changes to our valuation are as follows.

## Savolitinib

- We have updated our valuation for savolitinib in NSCLC to reflect changes in treatment paradigms since we initially modelled the indication. We forecast that globally there are 250,000 MET+ patients across first, second and third line. We believe HCM will initially focus on the second- and third-line setting but gradually move into first line. While savolitinib will be utilised as a monotherapy, particularly in the first line, we now forecast combinations with third- (Tagrisso) and first-generation EGFR inhibitors (Iressa/Tarceva) and/or chemotherapy. We have updated our probability of success for savolitinib from 50% to 75%.
- In China, we anticipate that HCM will be able to capture at peak 10% of the entire MET+ patients (c 6,000 NSCLC patients) across first and second line. While there is limited insurance coverage in China and a fragmented healthcare system (dependence on private payers), we believe this penetration rate is reasonable due to HCM's expertise in the market. We retain our price assumption in China of \$5,000 per month over an average one-year treatment course. At peak, we forecast sales in China of \$387m in 2027.
- Globally (ex-China), we forecast there to be approximately 190,000 NSCLC patients who are MET+ across first-, second- and third-line treatment. We anticipate HCM will achieve a peak penetration of 10% (c 19,000 patients). Different treatment dynamics in these markets,

particularly with the growing importance of Tagrisso following the impressive PFS presented in first-line patients (**18.9 months vs 10.2 months for current standard of care**) mean that, in our view, savolitinib is likely to be used in combination across all treatment lines. HCM's current clinical trials are focused on second- and third-line patients, where between 16% and 30% of EGFRm-resistant patients are MET+, respectively. We currently assume 16% of second-line patients are MET+ following first-generation EGFRm treatment with Iressa or Tarceva. However, with Tagrisso likely to move to a first-line therapy, this dynamic could change and result in increased numbers of second-line MET+ patients. We retain our price assumption globally of \$10,000 per month over an average one-year treatment course. At peak, we forecasts sales globally in NSCLC of \$2.5bn in 2026.

## Fruquintinib

- NSCLC: positive preliminary data presented at WCLC 2017 from an ongoing Phase II trial testing fruquintinib (VEGFR inhibitor) in combination with Iressa in first-line EGFR-mutant NSCLC support this unique VEGFR inhibitor's role in combination therapy. While a small number of patients were observed, the impressive efficacy supports our increased sales expectations for fruquintinib. Critically, our revised NSCLC numbers take into consideration fruquintinib use in earlier lines of treatment as combination therapy versus our original assumption of its use as monotherapy in third-line treatment. We now forecast HCM is able to capture 1.5% (c 9,000 patients) of the Chinese market. We forecast launch in China in 2020 (with peak sales of \$334m in 2024) and assume launch in the rest of the world in 2021 (with peak sales of \$721m in 2026).
- CRC: FRESCO CRC data underpin the hypothesis that fruquintinib's safety and efficacy profile could enable it to be positioned as best-in-class in China. HCM and partner Lilly submitted the NDA for third-line CRC to the CFDA in June 2017 and we anticipate the launch of fruquintinib in China in CRC in 2018. We have increased its probability of success to 90% from our original 75%.
- We increase our China pricing assumption to \$3,500 per month for all oncology indications. ROW pricing assumptions remain at \$5,000 per month. We note competitor product apatinib (jiansu HengRui Medicine) is priced at \$2,870 per month. We believe fruquintinib to be a superior product given it doesn't inhibit the CYP450 (whereas apatinib does).
- For ROW we remove the 11% royalty rate on sales and instead assume 100% of the economics are retained by HCM. We therefore upwardly revise our R&D costs for the ex-China clinical trial programs (that would necessitate an approval) and introduce sales and marketing costs (this includes cost to establish a clinical and regulatory team and other infrastructure) which will be required to support international commercial launch. In early years we model S&M as 50% to 70% of sales reducing to 20% of sales near peak penetration years.

## Other assets

- Increased epitinib probability of success in NSCLC with brain metastasis to 75% (from 30%) based on the soon-to-initiate Phase III clinical trial.
- For epitinib, thelatinib, sulfatinib and HMPL 523 we model full drug development and commercialisation costs are borne by HCM. We remove our illustrative 30% royalty on sales rate and forecast R&D and sales and marketing for each product. Given that HCM will have some infrastructure and reps employed to support fruquintinib launch we model incremental sales and marketing costs ranging from 10-30% upon initial launch and reducing in subsequent years.

It is worth noting that under US GAAP, jointly controlled entities are not consolidated proportionately, as these assets are now effectively off the balance sheet. For our valuation, this means the cash held by the jointly controlled entities is not included in our valuation of the group.

## Financials: Cash bolstered by secondary ADR issuance

FY17 results published in March 2018 highlighted robust net income growth within the CP division (CP continues to be HCM's primary profit and cash-generative division in the near term), coupled with clinical progress within the IP portfolio. Consolidated revenue at the group level in FY17 grew by 12% to \$241.2m (FY16: \$216.1m), with the IP division contributing \$36m (reflecting milestone payments, service fees and clinical trial reimbursement costs from partners) and consolidated CP sales contributing \$205.2m, up 13.4% vs FY16: \$180.9m. Full-year 2018 revenue guidance for the group of \$155-175m (we forecast \$163.6m) reflect in part changes to the sales model relating to the new CFDA two-invoice system roll out in China; while gross revenue amounts are affected, overall profit contribution from these business activities substantially remain unchanged. We expect the CP to continue to post double-digit net income growth in the near term; however, we note that the impact of the TIS and Guanbao divesture (as described before) will lead to lower reported top-line sales in 2018. Net profit growth, however, is expected to have minimal impact.

HCM has issued guidance for consolidated sales of \$115-125m in 2018 and net income of \$41-63m for the CP division. We forecast CP consolidated sales of \$115m in 2018 and \$129m in 2019, and net income of \$41.5m in 2018 and \$46.1m in 2019. These consolidated CP revenue numbers do not take into account revenues reported by the Shanghai Hutchison and Hutchison Baiyunshan joint ventures, as these are accounted for using the equity method; therefore, only the net attributable profit of the JV contribution is reported as equity in earnings of equity investees, net of tax below the PBT line.

We forecast IP revenues of \$48.6m in 2018 and \$51.1m in 2019, largely driven by developmental milestone payments from partners AZN and Lilly for progress of savolitinib and fruquintinib, respectively. HCM has guided \$40-50m in consolidated revenues for IP in 2018.

Profit before tax at the group level reported a loss of \$53.5m in FY17 (versus a loss of \$47.4m in FY16), R&D expenses increased significantly, reflecting investment throughout the portfolio (\$75.5m FY17 versus \$66.9m in FY16), S&M expenses increased to \$19.3m in FY17 (versus \$18.0m in FY16) and administrative expenses of \$24.0m (versus \$21.6m in FY16). We expect R&D expenses to increase to \$96.5m and \$124.5m in 2018 and 2019 (reported GAAP basis), respectively, reflecting the substantial need for investment in the burgeoning clinical trial programmes across the IP division, including the increased investment in savolitinib following the AZN deal amendment. Guidance for adjusted (non GAAP) R&D expenses stands at \$110-120m. The adjusted R&D expenses exclude the impact of the revenue received from external customers to the IP division, which is reinvested into clinical trials.

Guidance for 2018 stands at a net loss in the range of \$19-52m at the group level, variance in net income reflects unknown timing of one-time property gains (guidance \$0-20m) from Guangzhou land, the timing of which is subject to Guangzhou government policy. We forecast net losses at the group level of \$41.3m in 2018 and \$62.2m in 2019 (versus 2017 reported loss of \$26.7m).

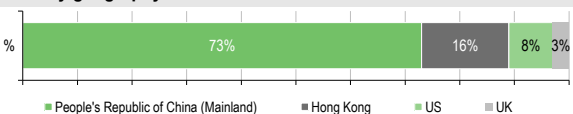
HCM reported a healthy cash position with available cash resources of \$479.6m (at 31 December) at the group level (cash and cash equivalents and short-term investments of \$358.3m, and unutilised bank borrowing facilities of \$121.3m). In October 2017, HCM raised \$301.3m (gross) (\$292.7m net) in new equity capital via a follow-on offering on NASDAQ.

**Exhibit 8: Financial summary**

	2015	2016	2017	2018e	2019e
December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
<b>PROFIT &amp; LOSS</b>					
Revenue	178,203	216,080	241,203	163,563	180,105
Cost of Sales	(110,777)	(156,328)	(175,820)	(89,900)	(94,632)
Gross Profit	67,426	59,752	65,383	73,663	85,473
Research and development	(47,368)	(66,871)	(75,523)	(96,500)	(124,500)
Other overheads	(29,829)	(39,578)	(43,277)	(45,353)	(51,260)
EBITDA	(7,756)	(44,264)	(50,692)	(63,690)	(83,909)
Operating Profit (before amort. and except.)	(9,771)	(46,697)	(53,417)	(68,190)	(90,287)
Intangible Amortisation	0	0	0	0	0
Operating Profit	(9,771)	(46,697)	(53,417)	(68,190)	(90,287)
Net Interest	(953)	(1,129)	(235)	227	208
Exceptionals	0	0	0	0	0
Profit Before Tax (norm)	(10,540)	(47,356)	(53,536)	(67,964)	(90,079)
Profit Before Tax (reported)	(10,540)	(47,356)	(53,536)	(67,964)	(90,079)
Tax	(1,605)	(4,331)	(3,080)	(3,000)	(4,504)
Equity investments, after tax	22,572	66,244	33,653	34,524	37,390
Profit After Tax (norm)	10,427	14,557	(22,963)	(36,440)	(57,192)
Profit After Tax (reported)	10,427	14,557	(22,963)	(36,440)	(57,192)
Minority	(2,434)	(2,859)	(3,774)	(4,900)	(5,000)
Discontinued operations	0	0	0	0	0
Net profit (norm)	7,993	11,698	(26,737)	(41,340)	(62,192)
Net profit (reported)	7,993	11,698	(26,737)	(41,340)	(62,192)
Average Number of Shares Outstanding (m)	54.7	59.7	61.7	66.5	66.5
EPS - normalised (c)	14.6	19.6	(43.3)	(62.1)	(93.5)
EPS - normalised and fully diluted (c)	14.6	19.5	(43.3)	(62.1)	(93.5)
EPS - (reported) (c)	14.6	19.6	(43.3)	(62.1)	(93.5)
Average number of ADS outstanding (m)	109.3	119.4	123.4	133.0	133.0
Earnings per ADS - normalised (\$)	0.07	0.10	(0.22)	(0.31)	(0.47)
Earnings per ADS (\$)	0.07	0.10	(0.22)	(0.31)	(0.47)
<b>BALANCE SHEET</b>					
Fixed Assets	140,087	175,057	165,737	177,761	195,774
Intangible Assets	3,903	3,606	3,738	3,513	3,194
Tangible Assets	8,507	9,954	14,220	21,945	32,886
Investments	127,677	161,497	147,779	152,303	159,694
Current Assets	89,675	167,380	432,195	391,682	300,515
Stocks	9,555	12,822	11,789	14,000	7,778
Debtors	38,628	49,349	53,566	76,659	93,231
Cash	31,949	79,431	85,265	79,479	65,962
St investments	0	24,270	273,031	213,000	125,000
Other	9,543	1,508	8,544	8,544	8,544
Current Liabilities	(81,062)	(95,119)	(104,600)	(115,256)	(101,294)
Creditors	(24,086)	(35,812)	(25,344)	(36,000)	(22,038)
Short term borrowings	(23,077)	(19,957)	(29,987)	(29,987)	(29,987)
Other	(33,899)	(39,350)	(49,269)	(49,269)	(49,269)
Long Term Liabilities	(46,415)	(43,258)	(8,366)	(8,366)	(8,366)
Long term borrowings	(26,923)	(26,830)	0	0	0
Other long term liabilities	(19,492)	(16,428)	(8,366)	(8,366)	(8,366)
Net Assets	102,285	204,060	484,966	445,821	386,629
Minority	(18,921)	(19,790)	(23,233)	(28,133)	(33,133)
Shareholder equity	83,364	184,270	461,733	417,688	353,496
<b>CASH FLOW</b>					
Operating Cash Flow	(9,385)	(9,569)	(8,943)	(51,112)	(82,517)
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(3,324)	(4,327)	(5,019)	(12,000)	(17,000)
Acquisitions/disposals	0	0	0	0	0
Dividends	(590)	(564)	(1,594)	(2,700)	(2,000)
Equity financing and capital movements	(1,676)	97,076	291,737	0	0
Other	12,179	(29,270)	(255,761)	60,026	88,000
Net Cash Flow	(2,796)	53,346	20,420	(5,786)	(13,517)
Opening net debt/(cash and ST investments)	2,085	18,051	(56,914)	(328,309)	(262,492)
Increase/(decrease) in ST investments	(12,179)	24,270	248,761	(60,031)	(88,000)
Other	(991)	(2,651)	2,214	0	0
Closing net debt/(cash and ST investments)	18,051	(56,914)	(328,309)	(262,492)	(160,975)

Source: Edison Investment Research, Company accounts.



<b>Contact details</b> 22nd floor, Hutchison House, 10 Harcourt Road, Hong Kong +852 2128 1188 www.chi-med.com	<b>Revenue by geography</b> 
<b>Management team</b> <b>Chairman: Simon To</b> Simon To is managing director and founder of Hutchison Whampoa (China), with over 30 years' service, having built the business from a small trading company to a large investment group with interests in aviation, hotels, port logistics, consumer products, residential developments, power plants and transport infrastructure. He is chair or director of a number of China-focused businesses and joint ventures. He has a BSc in mechanical engineering from Imperial College, London, and an MBA from Stanford.	<b>CEO: Christian Hogg</b> Christian Hogg joined the company in 2000 and has, as CEO, led all aspects of the creation, implementation and management of Hutchison China MedTech's strategy, operations in both the innovation and CPs, and London and New York IPOs. This included establishing research collaborations with AZN and Lilly and operating joint ventures with Nestlé, Hain Celestial, Shanghai Pharmaceuticals, Guangzhou Pharmaceuticals and Sinopharm. Previously, he spent 10 years with Procter & Gamble, including managing the detergent business in China and the global bleach business. He has a BSc in civil engineering from Edinburgh and an MBA from Tennessee.
<b>CFO: Johnny Cheng</b> Johnny Cheng has been CFO since 2008. Previously, he was VP finance of Bristol Myers Squibb in China and a director of Sino-American Shanghai Squibb Pharmaceuticals and BMS (China) Investment Co. He also spent eight years in various financial positions with Nestlé China and was an auditor with Price Waterhouse (Australia) and KPMG (Beijing). He has a bachelor of economics from the University of Adelaide and is a member of the Institute of Chartered Accountants in Australia.	<b>CSO: Weiguo Su</b> Weiguo Su is chief scientific officer, with 11 years' experience at the company. He created HCM's R&D strategy IP and led all pipeline discovery. Previous experience includes director of medicinal chemistry at Pfizer. He spent seven years at Harvard under E J Corey, the Nobel Prize winning medicinal chemist. Weiguo was one of the first mainland Chinese to be granted a scholarship to study at Harvard.
<b>Principal shareholders</b>	(%)
Hutchison Healthcare Holdings (wholly owned subsidiary of CK Hutchison Holdings)	60.3%
Mitsui & Co	4.8%
FIL Investment Managers (Singapore)	3.8%
<b>Companies named in this report</b> AstraZeneca (LON:AZN), CK Hutchison (SEHK:0001), Nestlé SA (VX:NESN), Guangzhou Baiyunshan (SHA: 600332, SEHK:874), Shanghai Pharmaceuticals (SHA: 601607, SEHK: 2607), Eli Lilly (LLY US)	

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