**Hutchison China MediTech**

Surufatinib on track for potential 2020 China approval

Hutchison China MediTech (Chi-Med) is one step closer to the commercialisation of its first wholly owned drug, surufatinib, in China. Early termination of the Phase III SANET-ep study in extra-pancreatic neuroendocrine tumours (epNET) - as it had already met its primary endpoint of progression-free survival (PFS) at the planned interim analysis - brings forward the timing of potential first surufatinib approval by c. 12 months. While full SANET-ep data will not be available until presentation at a future scientific conference, this result enables Chi-Med to seek a pre-NDA meeting with the China NMPA to discuss next steps in the regulatory process. Reviewing our surufatinib assumptions, we now assume a 2020 approval/launch in non-pancreatic NET. Our upgraded valuation is $5.14bn ($38.55/ADS) or £3.95bn (£5.93/share).

### Key Financials

<table>
<thead>
<tr>
<th>Year-end: December 31</th>
<th>2017</th>
<th>2018</th>
<th>2019E</th>
<th>2020E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales (US$m)</td>
<td>241.2</td>
<td>214.1</td>
<td>168.6</td>
<td>207.6</td>
</tr>
<tr>
<td>Adj. PBT (US$m)</td>
<td>(53.5)</td>
<td>(86.7)</td>
<td>(205.6)</td>
<td>(202.0)</td>
</tr>
<tr>
<td>Net Income (US$m)</td>
<td>(23.0)</td>
<td>(71.3)</td>
<td>(170.6)</td>
<td>(164.4)</td>
</tr>
<tr>
<td>Earnings per ADS (US$)</td>
<td>(0.22)</td>
<td>(0.57)</td>
<td>(1.31)</td>
<td>(1.26)</td>
</tr>
<tr>
<td>Cash (US$m)</td>
<td>358.3</td>
<td>301.0</td>
<td>285.9*</td>
<td>233.8</td>
</tr>
<tr>
<td>Adj. EBITDA (US$m)</td>
<td>(17.2)</td>
<td>(69.7)</td>
<td>(163.9)</td>
<td>(159.5)</td>
</tr>
</tbody>
</table>

**Source:** Trinity Delta  **Note:** Adjusted PBT excludes exceptional, Cash includes short-term investments, Adjusted EBITDA includes equity in earnings of equity investees.  *2019E cash figure includes assumed raise of $250m.

- **Potential for China NDA filing in 2020 and a 2021 launch**  The early stop of SANET-ep for efficacy expedites timelines for surufatinib in epNET. Extrapolating from fruquintinib regulatory and approval timelines for mCRC, we believe the China NDA for surufatinib could be submitted by end-2019, with NPMA approval possible c. 12 months later. Surufatinib is wholly owned by Chi-Med and will be marketed through its own China Oncology team and commercial infrastructure.

- **A wait for mPFS data release; 13.4 months in Phase II**  The pre-defined mPFS primary endpoint was met at the planned interim analysis of SANET-ep. Full data will be published at a scientific conference. For context, the Phase II study in NET (including both extra-pancreatic and pancreatic NET patients) rendered a 13.4 month mPFS in epNET. Compared with other tumour types, NETs are slow growing, associated with a longer duration of survival, with patients on therapy for longer.

- **Additional clinical data expected in 2019**  Multiple surufatinib clinical trials are ongoing or in planning, both as monotherapy or in combination with PD-1 inhibitors. As well as China NDA filing for epNET, interim analysis of the pivotal Phase III SANET-p trial (pancreatic NET) and submission for publication of results of the China Phase Ib/II biliary tract cancer (BTC) study are also anticipated in H219.

- **Updated valuation is £5.93/share and $38.55/ADS**  We employ a DCF-based SOTP approach that includes an rNPV of the clinical pipeline. Our revised valuation is $5.14bn ($38.55/ADS) or £3.95bn (£5.93/share). We highlight that this is a pre-money valuation pending the proposed Hong Kong IPO and global placement.

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**Company description**

Hutchison China MediTech is a Hong Kong headquartered biopharma with an established Commercial Platform in China, and a diverse pipeline of first-in-class/best-in-class selective oral tyrosine kinase inhibitors (Innovation Platform). Its pipeline, discovered in-house, is in development for the China and global oncology markets.

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Chi-Med: SANET-ep catalyses surufatinib timeline

Surufatinib is on track to become the first of Hutchison China MediTech’s (Chi-Med) wholly owned drugs to reach the market in China. The pivotal SANET-ep trial in advanced extra-pancreatic neuroendocrine tumours (epNET) has been stopped early for efficacy at the planned interim analysis following the IDMC (Independent Data Monitoring Committee) determination that the mPFS (median progression free survival) primary endpoint had been met. Full results will be presented at a future scientific conference. The next step for Chi-Med is a pre-NDA (new drug application) meeting with the China NMPA (National Medical Products Administration) to discuss the surufatinib NDA process. We believe that there is now potential for a 2019 NDA filing and 2020 approval for surufatinib in epNET. Updating our assumptions increases our valuation to $38.55/ADS ($5.14bn) or £5.93/share (£3.95bn) up from $35.57/ADS ($4.74bn) or £5.47/share (£3.65bn) previously.

Surufatinib (formerly HMPL-012 or sulfatinib) is Chi-Med's most advanced unpartnered asset and the company is prioritising securing a rapid first approval in China in all types of NET. NET is an umbrella term for tumours that develop from cells in the endocrine and nervous systems, most commonly in the digestive and respiratory tracts. It can be split into two distinct populations based on molecular genetics and treatment options. Non-(extra)-pancreatic NET (epNET) is the more common representing c90% of NETs; the remainder are pancreatic NET (pNET).

The pivotal 273-pt SANET-ep trial is the first NET study to complete. A second Phase III trial, SANET-p, in pNET, is enrolling with an interim analysis planned for late 2019. At this stage, we choose to err on the side of conservatism and assume no read through from the SANET-ep interim result to SANET-p.

Our base case assumption for SANET-ep was that it would run to completion, with full enrolment by end-2019 and top-line data in mid-2020. The interim stop for efficacy is a positive development, which, by our assessment results in a c 12 month benefit to timelines, suggesting NDA filing is likely in H219, with potential China launch by Chi-Med’s own commercial team in late-2020.

Fruquintinib experience informs new timeline assumption

The approval timeline for fruquintinib (Elunate), Chi-Med's first commercial product, provides a precedent which guides our revised assumptions for the surufatinib regulatory process. Fruquintinib was launched in 3L colorectal cancer (CRC) in November 2018 by partner Eli Lilly following NMPA approval in September 2018. The fruquintinib NDA was submitted within 4 months following top-line data from the pivotal FRESCO trial. It took a further 15 months for approval to be granted.

The earlier nature of SANET-ep data suggests some additional time (we assume an extra month) may be needed for Chi-Med to prepare the surufatinib NDA submission. However, as it will be manufactured at the same GMP certified facility in Suzhou as fruquintinib, we might expect a more rapid CMC review given that several components are already validated. Consequently, we presume this 15 month post-NDA approval timeline may be shorter for surufatinib.

Chi-Med is seeking first surufatinib approval in China for NET...

...SANET-ep interim stop for efficacy benefits timelines by 12 months...

...based on extrapolations from the fruquintinib regulatory process...

...which will also include some CMC overlap given a common manufacturing facility
SANET-ep mPFS data will be disclosed later...

...in Phase II, mPFS for epNET patients was 13.4 months on surufatinib.

SANET-ep data presentation pending

Chi-Med has not disclosed the mPFS achieved at the SANET-ep interim analysis, as trial data will be presented at a future scientific conference. A recap of the Phase II China NET data (summarised in Exhibit 1) gives an indication of the magnitude of response that might be expected. In particular, this trial reported a 13.4 month mPFS for the epNET population (n=40). While this is shorter than the 19.4 months for pNET patients (n=41) and 16.6 month mPFS for the overall trial (n=81), it does highlight that in general NETs are slow growing tumours compared with other tumour types. This means NETs are associated with a relatively long duration of survival, and NET patients are typically on drug therapy for longer.

Exhibit 1: Surufatinib China NET Phase II efficacy data

Source: Hutchison China MediTech, European Neuroendocrine Tumour Society 2017

epNET to be the first submission, with more to come

NET is the first of many opportunities for surufatinib. Its development programme is focused on indications with high unmet need and with the potential for a rapid path to market given the relative rarity of the cancer types targeted and limited treatment options.

Surufatinib is a novel selective oral small molecule TKI (tyrosine kinase inhibitor) with an angio-immuno kinase profile which differentiates it from other VEGFR (vascular endothelial growth factor receptor) TKIs. In addition to VEGFR, surufatinib targets FGFR (fibroblast growth factor receptor) and CSF-1R (Colony stimulating factor-1 receptor). This profile supports development both as a multi-functional monotherapy agent and in combination with checkpoint inhibitors. Ongoing and planned clinical trials for China and Global are presented in Exhibit 2.

Surufatinib’s ability to inhibit tumour associated macrophage (TAM) production facilitates generation of a PD-1 induced immune response. This feature is being explored under Chi-Med’s PD-1 monoclonal antibody collaborations (announced November 2018), which include a global partnership with Shanghai Junshi for Tuoyi (toripalimab), and a China-only deal with Taizhou Hanzhong for HX008.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Indication</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase III</strong>&lt;br&gt;SANET-p (China)</td>
<td>Pancreatic neuroendocrine tumours (NET)</td>
<td><strong>Status</strong>: Enrolment on track for completion early 2020, interim analysis expected late-2019. <strong>Design</strong>: Multi-centre, randomised (2:1), double-blind, placebo-controlled pivotal registration trial (n=195) of surufatinib 300mg once daily in unresectable/metastatic pancreatic NET. <strong>Endpoints</strong>: Primary endpoint is PFS; secondary endpoints include ORR, DCR, DoR, time to response, OS, safety and tolerability.</td>
</tr>
<tr>
<td><strong>Phase IIb/III</strong>&lt;br&gt;(China)</td>
<td>2L Biliary tract cancer (BTC)</td>
<td><strong>Status</strong>: Initiated in March 2019; top line data 2021. <strong>Design</strong>: Multi-centre, randomized (1:1), open-label, active control trial (n=298) of surufatinib 300mg once daily vs capcitabine in unresectable/metastatic BTC. <strong>Endpoints</strong>: Primary endpoint is OS; secondary endpoints include PFS, ORR, DCR, DoR, safety and tolerability.</td>
</tr>
<tr>
<td><strong>Phase III</strong>&lt;br&gt;(Global)</td>
<td>2L Pancreatic NET</td>
<td><strong>Status</strong>: 2L Sutent/Afinitor refractory pancreatic NET US/EU registration study in planning.</td>
</tr>
<tr>
<td><strong>Phase II</strong>&lt;br&gt;(China)</td>
<td>2L BTC</td>
<td><strong>Status</strong>: Enrollment complete; top line data likely to be published 2019. <strong>Design</strong>: Single-arm open label multi-centre POC study (n=32) of surufatinib in 2L BTC. Simon’s two-stage design: stage 1 (n=16) if ≤3 pts without progression or death at week 16 the study will be stopped, otherwise stage 2 will accrue an 16 additional patients. <strong>Endpoints</strong>: primary endpoint of PRS rate at week 16; secondary endpoints include safety/tolerability, vital signs, ORR, DCR, DoR, PFS, OS.</td>
</tr>
<tr>
<td><strong>Phase Ib/IIa</strong>&lt;br&gt;(Global)</td>
<td>Pancreatic NET and BTC</td>
<td><strong>Status</strong>: Phase II expansion (pancreatic NET) initiated July 2018. <strong>Design</strong>: Multi-centre, single-arm, open-label study to evaluate efficacy and safety of surufatinib monotherapy in patients with (a) 2L BTC and (b) advanced pancreatic NET. <strong>Endpoints</strong>: PFS, ORR, DCR, DoR, TTR, OS, and safety and tolerability.</td>
</tr>
<tr>
<td><strong>Phase I</strong>&lt;br&gt;(China)</td>
<td>Solid tumours</td>
<td><strong>Status</strong>: combination study with Tuoyi (PD-1) enrolling. <strong>Design</strong>: open label (n=24) Pase I study evaluating safety, tolerability, pharmacokinetics and efficacy of two surufatinib doses (200mg or 300mg) combined with Tuoyi in solid tumours. <strong>Endpoints</strong>: adverse events over 1 year and maximum tolerated dose (MTD) over 4 weeks.</td>
</tr>
<tr>
<td><strong>Phase I (US)</strong>&lt;br&gt;Solid tumours</td>
<td>Status: combination study with Tuoyi (PD-1) in planning.</td>
<td></td>
</tr>
<tr>
<td><strong>Phase I</strong>&lt;br&gt;(China)</td>
<td>Solid tumours</td>
<td>Status: combination sturdy with HX008 (PD-1) safety run-in in planning.</td>
</tr>
</tbody>
</table>

Source: Trinity Delta, Hutchison China MediTech, Clinicaltrials.gov  
Note: OS = overall survival, PFS = progression free survival, DCR = disease control rate, DoR = duration of response, TTR = time to response, ORR = overall response rate, POC = proof of concept

In addition to NDA filing for epNET, news flow for surufatinib during 2019 includes the interim analysis of the Phase III SANET-p trial, and the submission for publication of results of the China Phase IIb/II BTC study.

**An aside on fruquintinib...**

Fruquintinib is the first of Chi-Med’s internally developed TKIs to be approved and commercialised in China. Consequently, not only does it provides a guide for the potential regulatory timeline for surufatinib, but it is also a focus for investors and we use this opportunity to provide a brief status update.

We note that recent filings connected to Chi-Med’s proposed Hong Kong IPO provide unaudited Q119 revenues. These report ‘collaboration revenue’, ie royalty income from partner Eli Lilly in relation to fruquintinib. Royalty receipts stood at US$978k in Q119 vs US$261k in the first five weeks that fruquintinib...
NDRL inclusion would significantly increase revenues

Near term news flow anticipated from fruquintinib clinical trials

Valuation increases to $38.55 per ADS or £5.93 per share

Model will be updated again when the result of the HK IPO and global placement is known

was on the market (from November 2018). The growth in royalty income is a promising start; however, at present this is generated from out-of-pocket expenses supported by patient assistance programmes. We expect that once fruquintinib secures reimbursement on the National Reimbursement Drug List (NRLD) there will be a major inflection point in sales/royalties, although there is no firm guidance for when this may occur.

Like surufatinib, fruquintinib is in development for multiple tumour types, including in combination with checkpoint inhibitors. Various life cycle indications are in planning. Three tumour types have been or are currently being evaluated in Phase III, all of which should generate near-term newsflow.

- **Colorectal cancer**: Fruquintinib has launched in 3L mCRC in China; a Phase II/III US/EU study in mCRC is expected to initiate before end-2019.

- **Non-small cell lung cancer**: Full analysis of the China Phase III FALUCA trial in 3L NSCLC will likely be presented at a scientific conference during this year. As a reminder, FALUCA read out in November 2018; it missed its primary endpoint of overall survival but reached statistical significance in all secondary endpoints including PFS, objective response rate, disease control rate and duration of response.

- **Gastric cancer**: Following a planned interim analysis of the first c100 patients in H119, the IDMC advised that China Phase III FRUTIGA trial (in combination with paclitaxel) in 2L gastric cancer was advised to continue. Patient enrollment is expected to complete in 2020 and, since the primary end-point is event driven, top-line results could be seen by end-20 or, more probably, in early-21.

### Valuation

Clearly, the impressive outcome of the SANET-ep trial means that our forecast timelines for approval and marketing will be accelerated. We have reviewed our model to reflect the probable benefit of a c 12 months improvement in the surufatinib approval timelines compared to our previous expectations. We have also taken the opportunity to fine-tune our model for other relevant factors, most noticeably the current multiples for Chinese-listed healthcare companies.

The positive effect in our forecast time to approval (and hence launch) and the improvement in success probabilities (with the likelihood of success up from the 65% employed to reflect the previous Phase III status to the 90% we typically employ for pre-approval stages) comfortably offsets the small decrease in our valuation of the China Healthcare businesses. Our valuation methodology is detailed in our Initiation note (February 2019) and, as noted there, we strive to employ conservative assumptions throughout our valuations.

Updating our assumptions increases our valuation by 8.4% to $38.55/ADS ($5.14bn) or £5.93/share (£3.95bn) up from $35.57/ADS ($4.74bn) or £5.47/share (£3.65bn) previously. We would highlight that this is a pre-money valuation pending the proposed Hong Kong IPO and global placement. We will further update the model again once the result of the proposed fund-raise is known.
### CASH FLOW STATEMENTS

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Operating cash flow</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Net income</td>
<td>10,427</td>
<td>14,557</td>
<td>22,963</td>
<td>21,786</td>
<td>17,036</td>
<td>17,036</td>
</tr>
<tr>
<td>Non-cash adjustments &amp; other operating cash flow</td>
<td>9,863</td>
<td>27,557</td>
<td>28,525</td>
<td>31,276</td>
<td>8,340</td>
<td>10,227</td>
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<tr>
<td>Change in working capital</td>
<td>9,949</td>
<td>3,431</td>
<td>14,055</td>
<td>7,163</td>
<td>18,742</td>
<td>5,763</td>
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<tr>
<td><strong>Investing cash flow</strong></td>
<td>8,855</td>
<td>(33,597)</td>
<td>(260,780)</td>
<td>43,752</td>
<td>93,318</td>
<td>107,899</td>
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<tr>
<td>CAPEX</td>
<td>3,324</td>
<td>(4,327)</td>
<td>(5,019)</td>
<td>(6,364)</td>
<td>(6,682)</td>
<td>(7,016)</td>
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<td>Change in short term investments</td>
<td>12,179</td>
<td>(24,270)</td>
<td>(248,761)</td>
<td>58,116</td>
<td>100,000</td>
<td>114,915</td>
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<tr>
<td>Non-current liabilities</td>
<td>46,260</td>
<td>43,258</td>
<td>83,366</td>
<td>(34,384)</td>
<td>(34,384)</td>
<td>(34,384)</td>
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<tr>
<td>Long-term debt</td>
<td>26,768</td>
<td>26,830</td>
<td>0</td>
<td>(26,739)</td>
<td>(26,739)</td>
<td>(26,739)</td>
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<tr>
<td>Other non-current liabilities</td>
<td>19,492</td>
<td>(16,428)</td>
<td>(8,366)</td>
<td>(7,645)</td>
<td>(7,645)</td>
<td>(7,645)</td>
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<tr>
<td><strong>Equity</strong></td>
<td>102,277</td>
<td>204,060</td>
<td>484,966</td>
<td>412,255</td>
<td>251,668</td>
<td>97,726</td>
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</table>

Source: Company, Trinity Delta  Note: Adjusted numbers exclude exceptions. * Forecast EPS for 2019 and 2020 adjusted for one-to-one ordinary share split, with new ADS ratio of 1:5 shares. Our estimate of $250m proceeds from the proposed equity raise are shown as short-term debt in FY19e, until transaction size, structure, and terms are confirmed.
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