Trinity Delta

Hutchison China MediTech

Update

AACR 2019: Savolitinib in the spotlight in NSCLC

9 April 2019

Data at AACR from two key non-small cell lung cancer (NSCLC) trials has shown that savolitinib has encouraging anti-tumour activity and an acceptable safety profile both as monotherapy in exon 14m/del NSCLC, and in combination with osimertinib in MET+ EGFR-TKI refractory NSCLC. These presentations increase our confidence in Hutchison China MediTech (Chi-Med) and partner AstraZeneca's ability to launch savolitinib, as the first available selective c-Met inhibitor, in its respective NSCLC settings in 2021 (China: MET exon 14m/del) and 2022 (Global: in combination with osimertinib), subject to positive trial read outs and subsequent approvals. We upgrade our valuation to $35.57/ADS or £54.72/share.

Year-end: December 31	2017	2018	2019E	2020E
Sales (US$m)	241.2	214.1	168.6	207.6
Adj. PBT (US$m)	(53.5)	(86.7)	(205.6)	(204.5)
Net Income (US$m)	(23.0)	(71.3)	(170.6)	(166.9)
Earnings per ADS (US$)	(0.22)	(0.57)	(1.31)	(1.28)
Cash (US$m)	358.3	301.0	150.8	11.3
Adj. EBITDA (US$m)	(17.2)	(69.7)	(163.9)	(159.5)

Source: Trinity Delta Note: Adjusted PBT excludes exceptionals, Cash includes short-term investments, Adjusted EBITDA includes equity in earnings of equity investees.

- **TATTON B combo data shows acceptable risk-benefit profile** Globally, MET+ EGFR TKI resistant NSCLC is savolitinib's priority indication. MET amplification is a common resistance mechanism (20-30% of EGFRm NSCLC). TATTON B showed promising efficacy of the savolitinib/osimertinib combination in a heavily pre-treated population. For EGFR TKI T790M-/Met+ patients (post-gefitinib or erlotinib), the objective response rate (ORR) was 52% (24/46 partial responses) and 7.1 months duration of response (DoR). Osimertinib-resistant Met+ patients showed an 25% ORR (12/48 PRs) and median DoR of 9.7 months. Plans for further pivotal combination trials in NSCLC should be announced later in 2019. This is in addition to the ongoing SAVANNAH Phase II (c-Met+ 2L/3L EGFR/T790M refractory NSCLC), which is due to read out in 2021, and could support accelerated approval in the US.
- **China filing for 1L exon 14m/del NSCLC on track** Initial mid-trial data from the first 34 patients in the China Phase II exon 14m/del NSCLC study delivered a 39% ORR (PR in 12/31 evaluable patients), with >34 weeks median treatment duration. Enrolment of the full 50+ patients should complete in mid-H219 and subject to positive trial read out, China NDA filing is targeted for 2020.
- **Biomarkers to identify MET-driven tumours** Targeted therapies require patient selection. An AACR poster of the TATTON biomarker analysis highlighted challenges in defining MET selection criteria and assay reliability, and this combined with future clinical trials will help inform a new MET biomarker strategies.
- **We upgrade our valuation to $35.57/ADS or £54.72/share** We value Chi-Med using a DCF-based SOTP approach, which includes a clinical pipeline rNPV model, at $35.57/ADS or £54.72/share. This is an increase of $2.18/ADS or £3.20/share on our previous valuation and reflects Chi-Med's progress this year, including the recent start of the surufatinib China Phase IIb/III study in biliary tract cancer. Savolitinib represents 17%: $6.18/ADS ($824m) or £9.51/share (£634m) of our valuation.

Price (US ADS)	$31.78
(UK share)	4,675p
Market Cap	$4.24bn
	£3.12bn
Enterprise Value	$3.94bn
	£2.89bn
Shares in issue (ADS)	133.3m
(shares)	66.7m
12 month range	$20.83-$39.68
	3,180p-5,668p
Free float	32%
Exchanges	NASDAQ
	AIM
Sector	Healthcare
Company codes	HCM
	HCM.L
Corporate client	Yes

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: key NSCLC data at AACR

Hutchison China MediTech (Chi-Med) remains on track for near-term filings of savolitinib in China and globally in non-small cell lung cancer (NSCLC). Savolitinib has the potential to be the first approved selective cMet inhibitor in its respective NSCLC settings. Data from two key trials presented at AACR increase our confidence that anticipated filing and approval time lines for savolitinib will be met. We also upgrade our Chi-Med valuation to $4.742bn ($35.57/ADS) or £3.648bn (£54.72/share), previously $4.456bn ($33.49/ADS) or £3.428bn (£51.52/share). Of this, savolitinib represents 17% or $6.18/ADS ($824m) or £9.51/share (£634m). With rich news flow for 2019 and beyond, we anticipate future clinical, regulatory, and commercial catalysts will unlock further value.

AACR plenary session focused on NSCLC resistance mechanisms, including MET

Initial data from the China Phase II exon 14m/del NSCLC study of savolitinib monotherapy, and mature data from the savolitinib plus osimertinib combination in the 'B cohort' of the global Phase Ib/II TATTON trial were presented at AACR in a plenary session entitled 'Can the challenge of NSCLC resistance be MET or will we not MEK it?'. The following sections provide an overview of the data.

39% ORR in first 31 patients in China exon 14m/del NSCLC trial

To recap, Chi-Med and partner AstraZeneca intend to file a China NDA in 2020, assuming that data from the ongoing China >50-pt single arm Phase II study of savolitinib monotherapy in MET exon 14m/del NSCLC meets an agreed efficacy threshold. Initial data from the first 41 patients treated (31 of which were efficacy evaluable) was presented at AACR. As per the abstract, at December 2018, 12/31 patients evaluated had partial responses (39% objective response rate, ORR), with a median treatment duration of 34+ weeks. However, data presented had a later cut off (February 2019), with 16/31 PR (ORR of 51.6%), and a disease control rate of 93.5% (29/31).

Outside of China, data review from the dose expansion parts of the Phase Ib/II TATTON study (TATTON B and D) coupled to the outcome of regulatory discussions will determine pivotal trial design, dosing, and target patient populations for global savolitinib + osimertinib combination studies.

TATTON B data delivered 25% ORR and 9.7 months DoR for osimertinib-resistant MET+ patients

A potentially pivotal global Phase II study, SAVANNAH, evaluating savolitinib + osimertinib in c-Met+ 2L/3L EGFR/T790M refractory NSCLC is already underway, and due to read out in 2021. TATTON B data at AACR in a similar albeit not identical patient population (osimertinib approval in the 1L setting occurred after TATTON has initiated), showed a 25% ORR (12/48 partial responses) and a median duration of response of 9.7 months. Additional potentially pivotal NSCLC combination trials should be announced later in 2019.

TATTON (Part B): savolitinib/osimertinib combination

TATTON B: acceptable safety/tolerability and preliminary anti-tumour activity

Preliminary findings from the expansion phase (TATTON B) of the open-label, multi -centre Phase Ib TATTON study demonstrated that the combination of savolitinib (600mg QD) and osimertinib (80mg QD) in patients with EGFR-mutant, MET-amplified NSCLC has an acceptable safety/tolerability profile (primary objective) with preliminary anti-tumour activity (secondary objective).

AACR 2019 TATTON B data is comparable to WCLC 2017 presentations, but more mature

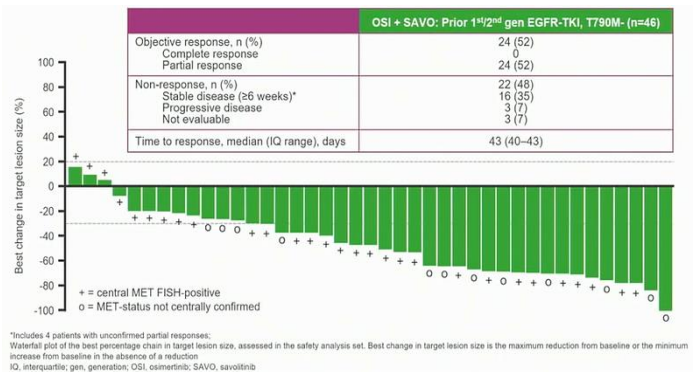
TATTON B data from two distinct patient populations that had failed prior EGFR TKI therapy were presented and are summarised in Exhibits 1 and 2. This efficacy data (ORR, PR) is broadly comparable with initial TATTON B data presented at WCLC 2017 (Exhibit 3), but includes more patients and the disclosure of duration of response data for both patient groups.

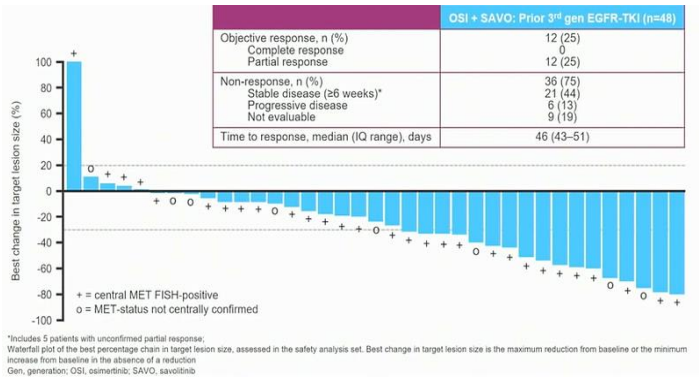
Exhibit 1: Preliminary anti-tumour activity and safety profile of savolitinib as shown by TATTON B data

Patient population	Prior treatment with 1st/2nd generation EGFR-TKI, T790M-/Met+ (n=46) (Abstract: CT032)	Prior treatment with a 3rd generation EGFR-TKI (n=48) (Abstract: CT033)
Objective response, n (%)	24 (52%)	12 (25%)
Complete response	0 (0%)	0 (0%)
Partial response	24 (52%)	12 (25%)
Non-response, n (%)	22 (48%)	36 (75%)
Stable disease (≥6 weeks)	16 (35%) [1]	21 (44%) [2]
Progressive disease	3 (7%)	6 (13%)
Non-evaluable	3 (7%)	9 (19%)
Time to response, median (IQ range), days	43 (40-43)	46 (43-51)
Duration of response, median (IQ range), months	7.1 (4.1-10.7)	9.7 (5.5-not calculable)
Any Grade ≥3 SAE, n (%)	25 (54%)	18 (38%)
Any SAE, n (%)	17 (37%)	14 (29%)
AE leading to discontinuation, n (%)		
Osimertinib	5 (11%)	5 (10%)
Savolitinib	16 (35%)	10 (21%)
Pts who discontinued, n (%)		
Both osimertinib and savolitinib	25 (54%)	31 (65%)
Savolitinib only	6 (13%)	-
Pts continuining on treatment at cut off	15 (33%)	17 (35%)

Source: Trinity Delta, Hutchison China MediTech. Note: Data cut off February 2018. IQ range = interquartile range. Stable disease includes: [1] 4 patients and [2] 5 patients with unconfirmed Partial Responses.

Exhibit 2: Waterfall plots of TATTON B data





Source: AACR 2019

Exhibit 3: Comparison of TATTON B efficacy data presented at WCLC 2017 and AACR 2019

Patient population	Prior treatment with 1st/2nd generation EGFR-TKI (T790M-/Met+)		Prior treatment with 3rd generation EGFR-TKI (MET+)	
	WCLC 2017	AACR 2019	WCLC 2017	AACR 2019
Number of patients	15	46	7	48
Objective response rate %	53%	52%	28%	25%
Number of Partial Responses	8	24	4	12

Source: Trinity Delta, Hutchison China MediTech. Note: WCLC data only includes patients with centrally confirmed cMet status. WCLC 2017 data cut off August 2017; AACR data cut off February 2018.

Acceptable safety profile in heavily pre-treated patient population…

The primary objective of TATTON B was safety/tolerability; the data supports an acceptable risk-benefit profile in what is a late-stage and heavily pre-treated patient population. The savolitinib + osimertinib combination did generate some additive toxicity, resulting in several treatment discontinuations. In addition, one of the two deaths (due to acute kidney injury) in the T790M-/MET+ cohort was possibly treatment related, although the principal investigator stated that it was 'difficult to evaluate'. Overall, the most frequent adverse events were nausea, vomiting, diarrhoea, and lowered leukocyte and platelet counts.

…with potential to refine savolitinib dose to optimise risk-benefit

We note that there is potential to manage this side-effect profile and reduce the 20-35% discontinuations due to adverse events, with a lower savolitinib dose. TATTON A, the dose-finding part of the study, established the 600mg savolitinib qd + 80mg osimertinib qd dose regime. The optimal dose may be lower. TATTON D is evaluating a meaningfully lower savolitinib dose of 300mg qd + 80mg osimertinib qd, and the Phase II SAVANNAH study has two dose levels: either savolitinib 300mg or 600mg qd in combination with 80mg osimertinib qd.

Efficacy as measured by RECIST criteria was the secondary object of the study. TATTON B yielded an ITT (intent to treat) ORR of 52% (24/46) for EGFR TKI T790M-/Met+ patients (post-gefitinib or erlotinib), with an efficacy evaluable ORR of 58% (24/42), with a median DoR of 7.1 months. In osimertinib-resistant Met+ patients the ORR for the ITT population was 25% (12/48), and the ORR for the efficacy evaluable population was 28% (12/43) as 5 patients were enrolled less than 8 weeks prior to cut off, with a median DoR of 9.7 months.

Promising efficacy suggests the savo/osi combo can overcome MET-driven resistance in EGFRM NSCLC

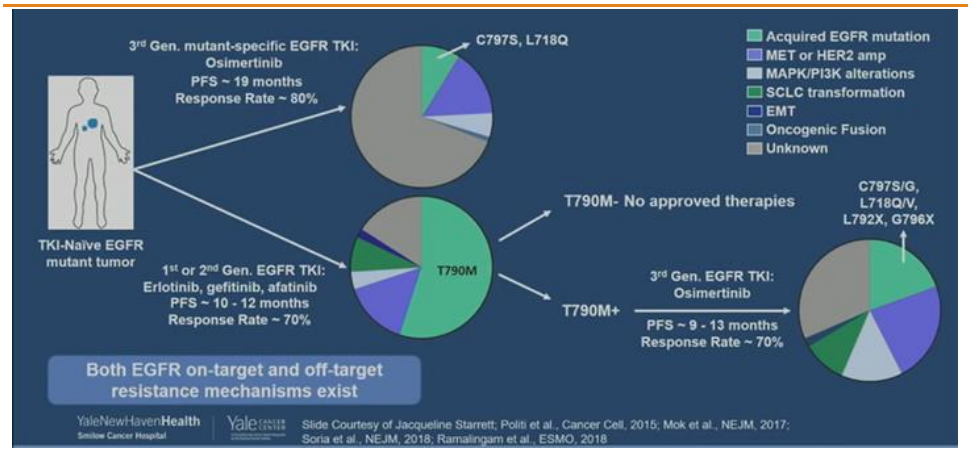
TATTON B data suggests that the savolitinib/osimertinib combination could offer an additional survival benefit as an effective targeted treatment option which can overcome MET-driven resistance mechanisms irrespective of prior EGFR-TKI therapy. Osimertinib was designed to provide a treatment option for EGFR T790M+ patients who have progressed after EGFR TKI therapy, but, as Exhibit 4 overleaf illustrates, c-met amplification is one of the most frequent acquired resistance mechanisms to osimertinib with 20-30% frequency (depending on whether is based analysis of circulating tumour cells or from tumour biopsy).

Standard of care in EGFR TKI resistant NSCLC with osimertinib approval in 1L after TATTON initiation

Osimertinib was approved in the 1L setting for EGFRm NSCLC after initiation of the TATTON study, thus only a subset of patients in the TATTON B cohorts received prior 1L osimertinib and developed MET-driven resistance. Increased 1L use of osimertinib will likely increase the addressable pool of c-Met+ patients.

A key challenge is developing a prospective MET biomarker strategy, with standardised MET patient selection criteria, and robust assays techniques. A poster at AACR summarising the TATTON biomarker analysis highlighted these issues, and concluded that this data could be combined with future clinical efficacy data to inform a prospective biomarker strategy to detect MET-driven EGFR-TKI resistance in NSCLC.

Exhibit 4: Mechanisms of resistance to osimertinib



Source: AACR 2019

SAVANNAH data in 2021 could support FDA filing in EGFRm MET+/T790M NSCLC patients

TATTON is an exploratory study. Randomised confirmatory trials would quantify the potential benefit and support a regulatory filing; however, they may not be necessary for an accelerated approval. The first potentially registrational trial, the 172-pt SAVANNAH Phase II, initiated in December 2018 and is investigating the savolitinib/osimertinib combination in EGFRm MET+ NSCLC patients who have progressed on osimertininb. This is evaluating a similar, albeit not identical population, to one of the cohorts in the TATTON study. Data is anticipated in 2021, which may be sufficient for a filing for accelerated approval.

China exon 14 m/del NSCLC: savolitinib monotherapy

Promising anti-tumour activity (including in brain metastases) and a tolerable side-effect profile was also confirmed by preliminary efficacy and safety data (abstract CT031) from the first 34 patients treated with savolitinib monotherapy in the China >50-pt single arm Phase II study in MET exon 14m/del NSCLC.

c50% ORR in first 31 patients in China exon 14m/del NSCLC trial, with medium treatment duration of >34 weeks

Of the first 34 patients treated (with a 17 December 2018 cut off), 17 were treatment-naïve, 13 were 2L, and 4 had ≥2 prior regimens. 31 patients were evaluated for efficacy. Tumour responses were rapid and durable, with 12/31 confirmed partial responses (PR), a 39% objective response rate (ORR). A further 4 PRs were yet to be confirmed; including these, the ORR rises to 52%. Of the remaining patients, 10 had stable disease, 2 showed disease progression, and 3 patients were unevaluable due to early discontinuation. Median treatment duration for confirmed PR was >34 weeks (16-96+ weeks).

Data presented at AACR had a later cut-off of 26 February 2019. This updated information showed 16/31 PR (ORR of 51.6%), with one unconfirmed response, and a disease control rate of 93.5% (29/31).

Savolitinib was generally well tolerated, with adverse events (AEs) mainly Grade 1/2, and most frequently nausea, peripheral oedema, increased liver enzymes, and vomiting. 12/34 (35%) of patients had Grade ≥3 AEs, with 5 (15%) discontinuing due to AEs, most commonly due to liver toxicity (6%).

Potential for first China approval in MET exon 14m/del NSCLC in 2021

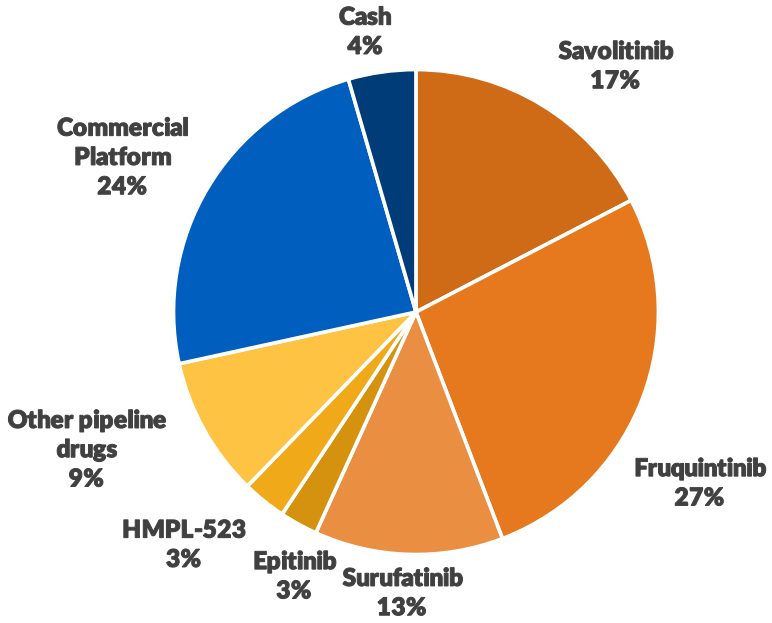
This study continues to enrol, with recruitment expected to complete in mid-H219. The primary endpoint is ORR, and should an agreed efficacy threshold be met, a China NDA will be filed in 2020 seeking accelerated approval.

Valuation

We value Chi-Med using a sum-of-the-parts model, incorporating an earnings-based multiple for the Commercial Platform and an rNPV analysis of the late-stage clinical pipeline for the Innovation Platform. The progress being seen across the businesses means we have raised our valuation to $4,742m (£3,638m), which is equivalent to $35.57 per ADS and £54.72 per share. For comparison, our previous valuation was $4,456m (equivalent to $33.49 per ADS) or £3,428m (£51.52 per share).

Exhibit 5 shows an overview of the relative importance of the various assets to the valuation; a description of our valuation methodology and a detailed breakdown its components can be found in our February 2019 initiation. Our valuation is split between the Innovation Platform, which contributes $3,394m or £2,610m, and the Commercial Platform, which adds $1,134m or £872m.

Exhibit 5: Relative contributions of Chi-Med programmes to valuation



Source: Trinity Delta

Scope for material uplifts in our valuation if progress continues

It is worth stressing that we employ conservative assumptions throughout our modelling; hence any number of incremental improvements on our base case scenarios (notably with the Innovation Platform) could result in sizeable uplifts in our valuation. It is also worth noting that this is a current valuation, based on the situation as we see it now, and not a price target for some time in the future. Often such price targets are expectations of what the share price should be, typically, in 12 months' time as various value inflection points are achieved. Such price targets run counter to our conservative approach; we strive to ensure our risk-adjusted models capture the various possible scenarios, relative to both upside and downside, and then we will update our valuations as the key points are reached. Although resulting in less dramatic upside potential, we believe our valuations are more realistic, attainable and, ultimately, credible.

Exhibit 6: Summary of financials

Year-end: December 31	$'000s	2016	2017	2018	2019E	2020E
INCOME STATEMENT						
Revenues		**216,080**	**241,203**	**214,109**	**168,560**	**207,569**
Cost of goods sold		(156,328)	(175,820)	(143,944)	(126,753)	(140,319)
Gross Profit		**59,752**	**65,383**	**70,165**	**41,807**	**67,250**
R&D expenses		(66,871)	(75,523)	(114,161)	(200,513)	(220,565)
Selling expenses		(17,998)	(19,322)	(17,736)	(13,419)	(14,416)
G&A expenses		(21,580)	(23,955)	(30,909)	(35,011)	(38,150)
Underlying operating profit		**(46,697)**	**(53,417)**	**(92,641)**	**(207,137)**	**(205,880)**
Other revenue/expenses		0	0	0	0	0
EBITDA		**(44,356)**	**(50,839)**	**(89,051)**	**(203,748)**	**(201,882)**
Operating Profit		**(46,697)**	**(53,417)**	**(92,641)**	**(207,137)**	**(205,880)**
Interest income/expense		(1,129)	(235)	4,969	555	359
Other income/expense		470	116	1,017	1,017	1,017
Profit Before Taxes		**(47,356)**	**(53,536)**	**(86,655)**	**(205,565)**	**(204,505)**
Adj. PBT		**(47,356)**	**(53,536)**	**(86,655)**	**(205,565)**	**(204,505)**
Current tax income		(4,331)	(3,080)	(3,964)	(4,839)	(4,805)
Equity in earnings of equity investees, net of tax		66,244	33,653	19,333	39,838	42,391
Net Income		**14,557**	**(22,963)**	**(71,286)**	**(170,565)**	**(166,918)**
Minority interests		(2,859)	(3,774)	(3,519)	(3,695)	(3,880)
Net income attributable to equityholders		**11,698**	**(26,737)**	**(74,805)**	**(174,260)**	**(170,798)**
EPS ($)		**0.20**	**(0.43)**	**(1.13)**	**(2.61)**	**(2.56)**
Earnings per ADS ($)		**0.10**	**(0.22)**	**(0.57)**	**(1.31)**	**(1.28)**
DPS ($)		**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Average no. of shares (m)		59.7	61.7	66.4	66.7	66.7
Gross margin		*28%*	*27%*	*33%*	*25%*	*32%*
EBITDA margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Underlying operating margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
BALANCE SHEET						
Current assets		**167,380**	**432,195**	**370,541**	**210,736**	**80,745**
Cash and cash equivalents		79,431	85,265	86,036	35,871	11,316
Short-term investments		24,270	273,031	214,915	114,915	0
Accounts receivable		45,035	42,270	42,958	36,945	45,495
Inventories		12,822	11,789	12,309	8,682	9,611
Other current assets		5,822	19,840	14,323	14,323	14,323
Non-current assets		**175,057**	**165,737**	**161,577**	**170,534**	**177,792**
Property, plant & equipment		9,954	14,220	16,616	19,923	22,955
Intangible assets		3,606	3,738	3,533	3,519	3,506
Investments in equity investees		158,506	144,237	138,318	143,982	148,221
Other non-current assets		2,991	3,542	3,110	3,110	3,110
Current liabilities		**(95,119)**	**(104,600)**	**(85,479)**	**(95,218)**	**(128,926)**
Short-term debt		(19,957)	(29,987)	0	0	(30,000)
Accounts payable		(35,538)	(24,365)	(25,625)	(34,727)	(38,443)
Other current liabilities		(39,624)	(50,248)	(59,854)	(60,491)	(60,483)
Non-current liabilities		**(43,258)**	**(8,366)**	**(34,384)**	**(34,384)**	**(34,384)**
Long-term debt		(26,830)	0	(26,739)	(26,739)	(26,739)
Other non-current liabilities		(16,428)	(8,366)	(7,645)	(7,645)	(7,645)
Equity		**204,060**	**484,966**	**412,255**	**251,668**	**95,226**
CASH FLOW STATEMENTS						
Operating cash flow		**(9,569)**	**(8,943)**	**(32,847)**	**(143,482)**	**(162,454)**
Net income		14,557	(22,963)	(71,286)	(170,565)	(166,918)
Non-cash adjustments & other operating cash flow		(27,557)	28,525	31,276	8,340	10,227
Change in working capital		3,431	(14,505)	7,163	18,742	(5,762)
Investing cash flow		**(33,597)**	**(260,780)**	**43,752**	**93,318**	**107,899**
CAPEX		(4,327)	(5,019)	(6,364)	(6,682)	(7,016)
Change in short term investments		(24,270)	(248,761)	58,116	100,000	114,915
Investment in an equity investee		(5,000)	(7,000)	(8,000)	0	0
Financing cash flow		**92,435**	**273,196**	**(8,231)**	**0**	**30,000**
Proceeds from equity		97,076	291,737	(2,322)	0	0
Increase in loans		(4,077)	(16,947)	(4,627)	0	30,000
Other financing cash flow		(564)	(1,594)	(1,282)	0	0
Net increase in cash		**49,269**	**3,473**	**2,674**	**(50,165)**	**(24,555)**
Exchange rate effects		(1,779)	2,361	(1,903)	0	0
Cash at start of year		31,941	79,431	85,265	86,036	35,871
Cash at end of year		**79,431**	**85,265**	**86,036**	**35,871**	**11,316**
Net cash at end of year		**56,914**	**328,309**	**274,212**	**124,047**	**(45,423)**

Source: Company, Trinity Delta Note: Adjusted numbers exclude exceptionals

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