EDISON

Trillium Therapeutics

US$55m financing extends runway and flexibility

Funding and quarterly update

Pharma & biotech

Trillium raised US$55.2m (gross) through an offering of 1.751m common shares and 1.078m convertible preferred shares, at US$19.50 per share. We believe Trillium can fund lead asset SIRPaFc through Phase II trials and it will expand preclinical SIRPaFc work in cancers beyond acute myeloid leukemia (AML). Data presented at AACR 2015 confirm that SIRPaFc does not bind CD47 on human red blood cells (hRBCs), aiding its safety profile.

Year end	Revenue (C$m)	PBT* (C$m)	EPS* (C$)	DPS (C$)	P/E (x)	Yield (%)
12/13	0.0	(3.7)	(2.69)	0.0	N/A	N/A
12/14	0.0	(12.3)	(2.92)	0.0	N/A	N/A
12/15e	0.0	(17.1)	(2.72)	0.0	N/A	N/A
12/16e	0.0	(17.4)	(2.54)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

AACR data confirms low hRBC-SIRPaFc binding

Trillium presented data at the 2015 American Association for Cancer Research (AACR) from 43 subjects showing that SIRPaFc binds poorly to human red blood cells (hRBCs) despite their high CD47 expression and their strong reactivity or binding with several different anti-CD47 monoclonal antibodies (mAbs). SIRPaFc has been shown to effectively bind to several AML cell lines, and hence the sparing of hRBC binding can reduce the risk for anaemia and improve drug targeting.

Celgene starts Phase I study on anti-CD47 mAb

As Trillium expects to start a Phase I SIRPaFc study in Q415, competing anti-CD47 products are entering the clinic. Celgene started in Q115 a 100-pt Phase I dose escalation study of CC-90002 (an anti-CD47 mAb) in patients with advanced, refractory solid and hematologic cancers; data is expected in late 2017. The Weissman group at Stanford University started a 36-pt study in August 2014 of its anti-CD47 mAb (Hu5F9-G4), with data expected in 2017. SIRPaFc's long term success could depend on its comparative safety/efficacy vs these competitors.

Financials: Likely funded through Phase II studies

Trillium had C$25.4m net cash as of 31 March 2015 and its trailing 12-month cash burn rate was C$10.8m. We expect the burn rate to increase when Trillium commences a Phase I AML study in Q415. Following the US$55.2m financing, we estimate Q215 net cash at C$86.0m. Assuming Trillium does not deploy significant capital in programmes other than SIRPaFc, we now estimate Trillium's funds on hand should last through the completion of a Phase II SIRPaFc trial, and into 2019. After including the full conversion of convertible preferred shares and a cash-neutral exercise (using the treasury method) of outstanding in-the-money options and warrants, we calculate 13.1m fully diluted (FD) shares outstanding, which would equate to a FD enterprise value of c US$220m.

20 May 2015

Price	**US$22.32**
Market cap	**US$152m**
	C$1.22/US$1
Net cash (C$m) at Q215e (including April 2015 financing)	86.0
Shares in issue	6.8m
Free float	30%
Code	TRIL/TR
Primary exchange	NASDAQ
Secondary exchange	TSX

Share price performance

%	1m	3m	12m
Abs	(15.2)	64.6	217.5
Rel (local)	(13.8)	65.2	204.8
52-week high/low	C$36.58		C$6.45

Business description

Trillium Therapeutics is a Canadian pharmaceutical company developing cancer therapeutics targeting immune-regulatory pathways that tumour cells exploit to evade the host immune system. Lead candidate SIRPaFc targets CD47 and is planned to start dosing in a Phase I study in AML in Q415.

Next events

File IND for SIRPaFc	Q315
Start patient dosing in Phase I SIRPaFc study	Q415

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Equity offering improves financial flexibility

In early April 2015, Trillium raised US$55.2m in gross proceeds through an underwritten public offering of common shares and non-voting convertible preferred shares. Trillium sold 1.751m common shares and 1.078m Series II convertible preferred shares,[1] at US$19.50 per share. Underwriting fees were 6% and additional expenses associated with the offering (eg legal and registration fees) were estimated by the firm at US$0.56m. Trillium indicated that net proceeds (which we estimate at US$51.3m) will be applied towards the development of lead candidate SIRPaFc in acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS), and other potential oncology indications; as well as for working capital and general corporate purposes. SIRPaFc targets an immune-regulatory pathway exploited by tumour cells to evade the host immune system. SIRPaFc is an antibody-like fusion protein that blocks the activity of CD47, a molecule that is up-regulated on cancer cells in AML and other tumours.

Prior to the equity financing, the company had indicated that it had sufficient resources (which reflected net cash and equivalents of C$25.4m on 31 March 2015) to fund its SIRPaFc through the initial Phase I study (planned to start in Q415 and which we estimate could take 12-18 months). We estimate that Trillium's strong share price performance year to date (the offering price was more than double Trillium's YE14 closing price) motivated management to take advantage of favourable market conditions to raise funds to further extend Trillium's runway and financial flexibility. The firm's previous capital raise took place in December 2013, when it raised C$33m in gross proceeds through a private placement.

Likely funded through Phase II SIRPaFc study

We estimate that Trillium's financial resources (post the offering) should be sufficient for the company to complete at least one Phase II study for SIRPaFc (assuming the planned Phase I study does not reveal unexpected toxicities or safety issues, and a Phase II trial enrolment target below 100 patients and costing under C$40m). Trillium's resources could be sufficient to allow it to pursue further R&D activities (in addition to funding the Phase II trial), which we believe will include expanding its preclinical programmes seeking validation for additional haematological or solid tumour indication targets for SIRPaFc. Trillium began a collaboration with academic investigators at the University of Western Ontario (London, Ontario) in August 2014 to explore the therapeutic potential of SIRPaFc, in a variety of solid and other liquid tumour models. It is also working with Toronto-area collaborators at University Health Network and the Hospital for Sick Children and expects to expand its collaboration network in 2015.

Seeking to validate SIRPaFc for indications beyond AML/MDS

We believe management is keen to demonstrate that SIRPaFc could provide clinical utility beyond AML.[2] This would strengthen the rationale that SIRPaFc could become a broad-based immunotherapy treatment for various cancers. By blocking CD47[3] from interacting with SIRPa, SIRPaFc impedes the survival mechanism (ie a 'do not eat' signal) whereby cells with high-CD47

[1] Convertible at any time to common shares on a one-for-one basis (subject to adjustments such as stock splits), at the option of the holder, subject to shareholder and exchange approvals if total shares outstanding held after conversion would exceed 19.99% of the then outstanding common shares.

[2] Both Trillium and researchers at other groups (notably Weissman and collaborators at Stanford University) have conducted numerous animal and xenograft studies demonstrating that CD47 blockage (through antibodies or fusion proteins) can reduce AML tumour burden.

[3] CD47 (Cluster of Differentiation 47) effectively normally sends a 'do not eat' signal to suppress phagocytosis by certain white blood cells including macrophages (thereby sparing CD47-presenting targets of clearance or removal).

membrane expression evade phagocytosis[4] by macrophages. CD47 is widely expressed on human cell surfaces and has been found to be over-expressed in many different tumour cells types,[5,6] including chronic lymphocytic leukaemia (CLL), mantle cell lymphoma, multiple myeloma (MM), ovarian cancer, glioma and glioblastoma.[7]

Phase I SIRPaFc study to be conducted in two parts

Following the completion of ongoing toxicology studies, Trillium intends to file an investigational new drug (IND) application in Q315 for a Phase I SIRPaFc study in patients with advanced hematologic malignancies. Recruitment is planned to begin in Q415 and the study will be conducted in two parts. Patients with relatively normal bone marrow function and peripheral blood parameters will be recruited initially to assess overall SIRPaFc tolerability and haematological effects, before subsequently enrolling patients who may have compromised marrow function.

Potential for re-visiting CD200 mAb, other initiatives?

Trillium may have increased flexibility to pursue the acquisition of new pipeline assets or resume R&D development on its existing assets that had been de-emphasized while the firm had been focusing resources on SIRPaFc. Trillium has rights to a human monoclonal antibody (mAb) that blocks CD200, an immunosuppressive molecule overexpressed by many hematopoietic (blood cell related) and solid tumours and believed to be employed to evade immune attack. Trillium believes CD200 overexpression correlates with more rapid disease progression. Trillium's anti-CD200 antibodies have promoted anti-tumour activity in a human tumour xenograft model. This programme is ready to enter a formal pre-clinical program, but had been suspended internally since mid-2013 due to a prioritization of company resources towards SIRPaFc. The company's formal position is that it is seeking a development partner to advance this programme into IND-enabling studies.

Exhibit 1: Trillium Therapeutics' product pipeline

Product	Description	Stage
TTI-621 (SIRPaFc)	Oncology including acute myeloid leukaemia	Preclinical
TTI-622 (SIRPaFc)	Cancer (combination therapy)	Preclinical
CD200 Monoclonal antibody	Cancer	Preclinical (on hold)

Source: Edison Investment Research

Trillium provides additional RBC sparing data at AACR 2015

On 21 April 2015, at the American Association for Cancer Research (AACR) meeting, Trillium presented data from an expanded pool of blood donors (n=43) that showed that SIRPaFc binds poorly to hRBCs despite their high CD47 expression and their strong reactivity or binding with several different anti-CD47 mAbs. Trillium previously showed (AACR 2014) that SIRPaFc binds effectively to several AML cell lines. This poor SIRPaFc-hRBC binding pattern is independent of gender, blood type (A/B/O) or Rh status.

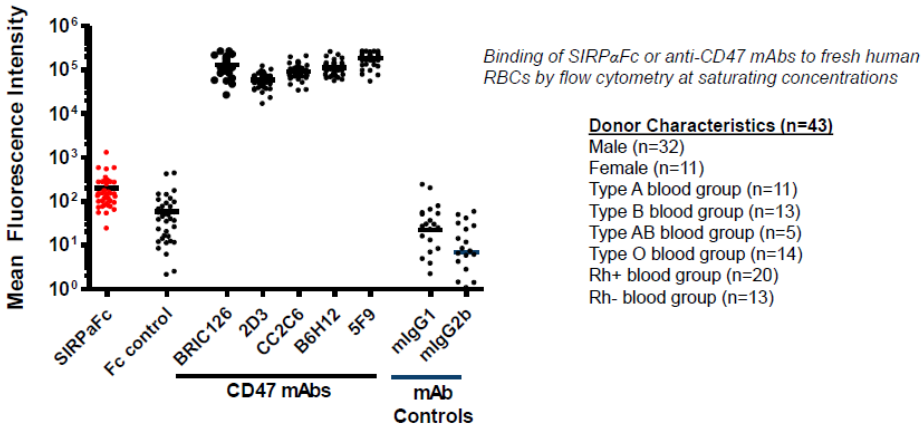
[4] A progress by which a phagocytic cell (such as certain white blood cells) engulfs a targeted foreign particle or material, forming an internal vesicle, which is then digested.

[5] Expert Opin Ther Targets. 2013 January; 17(1): 89–103.

[6] Elevated CD47 expression has been reported in a variety of cancers including renal and prostate carcinoma, multiple myeloma (MM), T-cell acute lymphoblastic leukaemia (ALL), oral squamous cell carcinoma, human acute myeloid leukaemia-associated stem cells, bladder carcinoma cells, glioma and glioblastoma.

[7] Willingham et al. 2012 PNAS 109:6662.

Exhibit 2: Human SIRPaFc binds very poorly to CD47+ hRBCs



Source: Trillium poster presented at 2015 AACR meeting

SIRPaFc nonetheless binds RBCs from other species, and induces clinically significant anaemia in monkeys after intravenous administration. This suggests that agents that bind CD47 present on hRBCs (such as the tested mAbs) could potentially provoke increased phagocytosis of such cells and thus undesired haematological toxicity risk (eg, anaemia).

Trillium determined that the failure of SIRPaFc to bind hRBCs correlates with the presence of detergent-insoluble CD47 in hRBC membranes, which is consistent with a proposed model suggesting that CD47 mobility is required to form high affinity binding clusters with SIRPaFc.

Wide CD47 expression on hRBCs can possibly also act as a large 'antigen sink' for potential therapies targeting CD47 (ie increasing the amount of drug needed to reach targeted sites), if they bind to such hRBCs. The presented data suggest the relative sparing on CD47-binding on hRBCs by SIRPaFc could lead to it being a superior CD47-targeting therapeutic relative to alternative approaches given a possibly reduced likelihood of hRBC sink effects (thus leading to potentially improved pharmacokinetics) and causing hRBC toxicities. However, InhibRx reports that its anti-CD47 mAb, INBRX-103 (in-licensed to Celgene and also termed CC-90002) has a positive preclinical safety profile distinct from other CD47-targeting mAbs, with no RBC hemagglutination or RBC depletion, and no toxicity in high dose primate studies. We expect further data on human safety (including anaemia-risks) profiles of the anti-CD47 mAbs in clinical development (eg.CC-90002 and Stanford's Hu5F9-G4) to become more visible as their clinical trials proceed.

Celgene brings its CD47 mAb to clinic

In Q115, Celgene (NASDAQ: CELG) started an open-label Phase I dose escalation study (NCT02367196) of CC-90002 (an anti-CD47 mAb in-licensed from privately held InhibRx), administered by intravenous (IV) infusion, in patients with advanced, refractory solid and hematologic cancers. Three US sites are currently enlisted in the study, and Celgene plans to recruit 100 patients and complete the trial in late 2017. While the primary objective is to establish the maximum tolerated dose (MTD) and dose-limiting toxicity, secondary endpoints will include measures of anti-tumour efficacy and pharmacokinetics.

The Weissman group at Stanford University is developing its anti-CD47 antibody (Hu5F9-G4) as a potential cancer drug, and in August 2014 started a 36-patient Phase I safety study (NCT02216409) in patients with advanced solid tumours. Results are expected in August 2017. The California

Institute for Regenerative Medicine,[8] is one of the study sponsors, and the trial is designed to determine the MTD and optimal dosing regimen of the anti-CD47 antibody.

Privately-held Novimmune is developing NI-1701, a bi-specific antibody that seeks to block CD47 while also having a Fab targeting arm that is selective for CD19 (an antigen more highly expressed in tumours), although this is currently in discovery stages, with clinical trial applications planned for H216.

Exhibit 3: Competitors developing anti-cancer compounds targeting CD47

Company name	Description	Development stage
Weissman Group (Stanford)	Anti-CD47 monoclonal antibody	Phase I
Celgene/InhibRx	Anti-CD47 monoclonal antibody	Phase I
Novimmune	Anti-CD47 and CD19 Bi-specific antibody	Discovery

Source: Edison Investment Research

Financials

Trillium had C$25.4m net cash at 31 March 2015 (C$25.7m cash and marketable securities, offset by C$0.3m debt) and the trailing 12-month cash burn rate was C$10.8m. We expect the burn rate to increase when Trillium commences a Phase I AML study in Q415.

Assuming the company does not deploy proceeds into additional programmes beyond SIRPaFc or product acquisitions, we now estimate Trillium's funds on hand should last through the completion of a Phase II SIRPaFc trial, and into 2019. Prior to the April financing, the firm had indicated that its objective was to partner or out-license SIRPaFc upon the completion of Phase II studies; the company now has a sufficiently strong financial position to enable it to pursue this strategy without requiring additional capital. If Trillium seeks to raise further funds in coming years, at deal sizes comparable to the April 2015 offering, it could be in a position to independently fund a Phase III pivotal study. Completing a Phase III study could allow Trillium to retain a higher share of future SIRPaFc economics than would be assumed, if the company were to transact or out-license the asset after Phase II.

Our FD common share count post-the April 2015 financing of 13.1m shares is based on the 5.04m listed basic shares outstanding as of 31 March 2015 (as per regulatory filings), and includes the addition of 1.75m common shares from the April 2015 offering, 3.24m from preferred share conversion (1.078m Series II preferred shares from the 2015 offering convertible one-for-one into common shares, and 64.9m existing Series I preferred shares convertible into 2.16m common shares) and 3.04m shares through the cash-neutral exercise (using the treasury method) of outstanding in-the-money options and warrants.

[8] http://www.cirm.ca.gov/our-progress/awards/clinical-investigation-humanized-anti-cd47-antibody-targeting-cancer-stem-cells.

Exhibit 4: Financial summary

C$(000)	2013	2014	2015e	2016e	2017e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
General & Administrative	(962)	(2,577)	(2,253)	(2,299)	(2,345)
Research & Development	(2,688)	(9,938)	(15,714)	(16,400)	(16,000)
EBITDA	(3,650)	(12,515)	(17,967)	(18,699)	(18,345)
Depreciation	(16)	(47)	(84)	(114)	(153)
Amortization	(633)	(611)	(219)	(102)	(53)
Operating Profit (before exceptionals)	(4,299)	(13,173)	(18,270)	(18,915)	(18,551)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(4,299)	(13,173)	(18,270)	(18,915)	(18,551)
Net Interest	10	291	918	1,446	1,070
Profit Before Tax (norm)	(3,657)	(12,271)	(17,133)	(17,367)	(17,427)
Profit Before Tax (FRS 3)	(4,289)	(12,882)	(17,352)	(17,469)	(17,481)
Tax	0	0	0	0	0
Profit After Tax and minority interests (norm)	(3,657)	(12,271)	(17,133)	(17,367)	(17,427)
Profit After Tax and minority interests (FRS 3)	(4,289)	(12,882)	(17,352)	(17,469)	(17,481)
Average Number of Shares Outstanding (m)	1.4	4.2	6.3	6.8	6.9
EPS - normalised (C$)	(2.69)	(2.92)	(2.72)	(2.54)	(2.53)
EPS - normalised and fully diluted (C$)	(2.69)	(2.92)	(2.72)	(2.54)	(2.53)
EPS - (IFRS) (C$)	(3.16)	(3.06)	(2.76)	(2.55)	(2.53)
Dividend per share (C$)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	1,582	668	618	680	779
Intangible Assets	1,473	433	214	112	58
Tangible Assets	109	235	404	568	721
Current Assets	33,505	27,518	79,880	63,623	44,114
Short-term investments	527	0	0	0	0
Cash	32,457	26,165	78,680	62,423	42,914
Other	522	1,353	1,200	1,200	1,200
Current Liabilities	(733)	(3,528)	(3,533)	(3,533)	(305)
Creditors	(733)	(3,528)	(3,533)	(3,533)	(305)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(446)	(353)	(340)	(340)	(340)
Long term borrowings	(446)	(353)	(340)	(340)	(340)
Other long term liabilities	0	0	0	0	0
Net Assets	33,908	24,304	76,625	60,430	44,248
CASH FLOW					
Operating Cash Flow	(2,492)	(7,740)	(16,543)	(17,425)	(20,273)
Net Interest	10	291	918	1,446	1,070
Tax	0	0	0	0	0
Capex	(34)	(174)	(253)	(278)	(306)
Acquisitions/disposals	(648)	0	0	0	0
Financing	34,030	966	68,424	0	0
Net Cash Flow	30,865	(6,655)	52,547	(16,257)	(19,509)
Opening net debt/(cash)	(1,375)	(32,537)	(25,812)	(78,340)	(62,083)
HP finance leases initiated	0	0	0	0	0
Other	297	(70)	(19)	0	0
Closing net debt/(cash)	(32,537)	(25,812)	(78,340)	(62,083)	(42,574)

Source: Company reports, Edison Investment Research

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