INITIATING COVERAGE
Biotechnology
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Simos Simeonidis, Ph.D.
simos.simeonidis@cowen.com 646.562.1386
Yatin Suneja
yatin.suneja@cowen.com 646.562.1388
Raymond Chang, M.D.
raymond.chang@cowen.com 646.562.1337

FATE THERAPEUTICS, INC. (NASDAQ:FATE)

Initiation: A Better Fate for Stem Cell Transplantation

Recommendation

Rating:	Outperform
Price Target (in $):	NA
Dividend:	NA
Enterprise Value (MM):	$98.0

Earnings Per Share

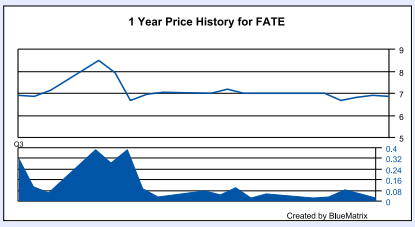
	2012A	2013E	2014E
Q1	--	--	*$(0.36)*
Q2	--	--	*$(0.38)*
Q3	--	*$(0.41)*	*$(0.38)*
Q4	--	*$(0.30)*	*$(0.37)*
FY	*$(13.06)*	*$(1.78)*	*$(1.49)*

Stock Statistics as of 10/25/2013 (in $)

Price:	$6.87
52W Range:	$9.19-$6.06
Shares Out (MM):	22.2
Market Cap (MM):	$153.0
Net Debt (MM):	$2.8
Net Cash Per Share:	$2.47

Fundamentals

Revenue (MM) ('12A)	2.7
Revenue (MM) ('13E)	0.8
Revenue (MM) ('14E)	0.0



We are initiating coverage of Fate Therapeutics with an Outperform rating.

ProHema: better outcomes for patients undergoing stem cell transplantation

Fate's lead program is ProHema, a cell therapy product for patients undergoing hematopoietic stem cell transplantation (HSCT). By optimizing hematopoietic stem cells (HSC) *ex vivo*, treatment with ProHema in early trials resulted in improved homing and engraftment of cells. Fate will start a Phase II trial in adults undergoing HSCT for hematologic malignancies (1H14), and two pediatric trials in hematology (mid-14) and lysosomal storage disorders (2H14).

What's the commercial opportunity for ProHema?

There are 8K allogeneic HSCTs in the US, and another 15K in the EU each year, and 15-20% of these use umbilical cord blood (UC) as their source. If successfully developed, ProHema can gain significant share in the UC-derived market. Assuming a conservative 16% penetration rate in the allogeneic HSCT market, we estimate ProHema can be a $360M US/EU product in 2025, with peak $515M 2030 sales. These revenue numbers do not account for upside that exists should ProHema and follow-on products manage to demonstrate utility in rare genetic disorders where transplantation is emerging as a potential treatment option.

Wnt7a work is very early, but may have the most upside potential

Fate is also developing *in vivo* modulators of muscle satellite stem cells (SSC). Preclinical work has shown administration of a recombinant Wnt7a analog leads to expansion of SSCs and improves muscle's regenerative capacity. These data have obvious implications and potential in the treatment of muscular dystrophies. Fate plans to select a drug candidate in 4Q13 and start clinical development in DMD in 2015. With obvious caveat that this work is still in its very early stages, a look at DMD company valuations highlights both the commercial potential and investor interest.

Please see addendum of this report for important disclosures.

Company Description

Fate Therapeutics is a biotechnology company developing pharmacologic modulators of adult stem cells for the treatment of difficult to treat, orphan diseases. Fate's hematopoietic stem cell (HSC) modulation platform is focused on the *ex vivo* optimization of HSCs used in allogeneic stem cell transplantation (HSCT). Fate's lead program is ProHema, a HSC therapeutic produced by pharmacologic modulation of umbilical cord blood, which is currently in Phase II development for hematologic malignancies in adult patients. The company plans to investigate ProHema in the pediatric population for indications in hematologic malignancies (mid-2014) and rare, genetic lysosomal storage disorders (LSDs) (2H14). Fate is also developing an *in vivo* modulation strategy for muscle stem cells, known as satellite stem cells (SSC), using a Wnt7a therapeutic to improve muscle regeneration, with application in treatment of muscular dystrophies. This program is in preclinical development, with selection of the Wnt7a drug candidate expected in 4Q13 and IND submission anticipated by YE14. Fate was founded in 2007 and went public in October 2013. The company is headquartered in San Diego, CA and has 33 employees.

Fate: R&D Pipeline

Candidate name	Indication	P-C	I	II	III	FILING	MKT	Comments
HSC Modulation Platform								
ProHema	Adult hematologic malignancies			•				Resume enrollment in Phase II ProHema-03 trial, 1H14
ProHema	Pediatric hematologic malignancies	•						Initiate a Phase Ib trial in pediatric population, mid-14
ProHema	Lysosomal storage disorders	•						Initiate a Phase I trial in pediatric population, 2H14
2nd-generation HSC Therapeutic	Lysosomal storage disorders	•						-
SSC Modulation Platform								
Wnt7a Protein Analogs	Muscular dystrophies	•						Submit IND application YE14
Wnt7a Protein Analogs	Neuromuscular disorders	•						-
Total Drugs in Development		**5**	**0**	**1**	**0**	**0**	**0**	
San Diego, CA	**Investor Relations Contact: Paul Cox - 212.362.1200**							

Source: Cowen and Company

Fate: Expected Milestones

Milestones	Timing
ProHema	
Resume enrollment in the Phase II ProHema-03 trial with new media in adults	1H14
Initiate Phase Ib trial of ProHema in pediatric patients	mid-2014
Initiate Phase I trial of ProHema in lysosomal storage disorders (LSDs)	2H14
Data from Phase II ProHema-03 trial of ProHema in adults	***mid-2015***
Data from Phase Ib trial of ProHema in pediatric patients	2015
Initiate Phase III trial of ProHema in adults/pediatric patients	2H15
Wnt7a	
Select Wnt7a drug candidate	4Q13
Submit IND application for Wnt7a	YE14
Initiate Phase Ia dose exploration trial of Wnt7a in healthy volunteers	2015
Data from a Phase Ia dose exploration trial of Wnt7a in healthy volunteers	1H15
Initiate Phase Ib multi-dose trial of Wnt7a in DMD patients	2H15

Source: Cowen and Company

Investment Thesis

We are initiating coverage of Fate Therapeutics with an Outperform rating. Our thesis on FATE is based on the company's core technology and expertise in the pharmacologic modulation of adult stem cells for the development of therapeutics for treatment of orphan diseases.

ProHema: better outcomes for patients undergoing stem cell transplantation. Fate's deep expertise in and understanding of stem cell biology has culminated in the development of ProHema, a cell therapy product for use in patients undergoing hematopoietic stem cell transplantation (HSCT) for hematologic malignancies. The concept behind the development of ProHema is that small molecule modulators can potentially be added to unmodulated hematopoietic stem cells (HSCs) before a HSCT, thereby improving the safety profile and the outcome of the procedure. By pharmacologically optimizing HSCs *ex vivo*, in preclinical experiments, treatment with ProHema resulted in doubling in the "homing" of transplanted cells to the marrow and quadrupling of their engraftment. Results from the first Phase I clinical trial of ProHema in 12 patients were equally promising, with improvements in median time to engraftment, % engrafted, and overall outcomes. The company is now planning to initiate a Phase II trial in adult patients undergoing HSCT for hematologic malignancies in 1H14. In addition, the company is planning on conducting two pediatric trials in 2014: the first one in patients undergoing HSCT for hematologic malignancies, expected to start in mid-2014, and the second one in patients undergoing HSCT to treat lysosomal storage disorders (LSDs), expected to start in 2H14.

The tangible commercial opportunity for ProHema…There are approximately 8,000 allogeneic HSCTs performed in the US each year, and another 15,000 in the EU. Approximately 15-20% of these procedures use umbilical cord blood as their source, which is the setting Fate has used for its trials thus far and will be using for its Phase II trial. If successful in its Phase II and Phase III development, we estimate that ProHema can gain significant share in the umbilical cord blood-derived HSCT market, along with share in the bone marrow- and peripheral blood-derived markets as well. Using conservative market penetration assumptions for ProHema (*16% of the overall allogeneic HSCT market*), we project that it can be a $360M US/EU product in 2025, with peak US/EU sales of ~$515M in 2030.

…and the potential upside: These revenue numbers do not account for the upside that exists, should ProHema and follow-on products manage to demonstrate utility in rare genetic disorders for which transplantation is not currently used as the standard of care, but is being used investigationally, and is starting to emerge as a potential treatment option. In addition, and as shown on page 12, we have performed a scenario analysis, evaluating a number of alternative launch trajectories which result in different peak market penetrations, translating into significant revenue projections for ProHema. For simplicity, we have only looked at the allogeneic HSCT market in its steady state today, i.e., we have not increased the use of HSCTs significantly. Furthermore, we have kept the number of umbilical cord blood transplants as a proportion of the overall HSCT market steady, and have not increased the number of UCB-derived procedures, even though a number of sources indicate that the UCB portion of the market may be growing. Despite this conservative approach, it is clear that should

ProHema succeed in its clinical development program, it could become a very successful commercial product, even by achieving modest market penetration, and without counting on significant market or umbilical cord blood segment growth.

Our consultants are positive on ProHema for hematologic malignancies: In order to get a better understanding of the ProHema clinical development program and its clinical and commercial potential, we consulted with five hematologist/oncologists specializing in HSCT at major, leading transplantation centers across the US. This group included specialists in both adult and pediatric stem cell transplantation. All of our consultants had significant clinical practices including allogeneic HSCT and the use of umbilical cord blood as a cell source. Additionally, each of our experts was familiar with ProHema, and some were participants in ProHema clinical trials. Our consultants view ProHema as easy to use (*"rather straightforward," "a very simple type of technique," "practical, not at all problematic"*). With regard to the ProHema data, all of our experts noted the early nature of the results, but did feel that the data were "*interesting*" and *"promising."* In particular, they appeared to be intrigued by the underlying strategy of ProHema modulation for homing enhancement, and differentiated this from other approaches focused on *ex vivo* expansion of cord blood cells, which were viewed generally as "*laborious,*" "*expensive,*" and "*time-consuming.*" While all our consultants did view the preliminary ProHema data to have potential, the group was somewhat split on the strength of the clinical results thus far, in particular regarding the reduction in time to neutrophil engraftment reported in the Phase I trial (compared to historical control). On the one hand, there were a couple physicians who viewed the reduction in engraftment time of 3-4 days as *"clinically meaningful,"* given that the longer amount of time a patient is neutropenic leads to an increased risk of transplant-related morbidity. They felt that this improvement would reduce length of stay in the hospital, leading to relative risk reduction for the patient, as well as potential cost savings (a meaningful economic benefit). On the other hand, there were two physicians in our group who questioned the impact, stating *"I'm not sure if 3 days is overall meaningful"* and asking, *"is it meaningful in terms of death and infections?"* Overall, our consultants felt that there is a *"reasonable"* chance of a successful ProHema clinical trial program and ultimately approval, if meaningful improvements can be demonstrated in hematopoietic recovery. One of our experts remarked that knowing Fate is working with the FDA on design of a trial which will support an approval pathway provides further confidence. In terms of potential uptake of ProHema, if approved, our physicians were aligned in expressing a reasonable chance of adoption as well.

ProHema for Rare Genetic Disorders. In addition to the use of ProHema in patients undergoing HSCT for hematologic malignancies, Fate is also pursuing the potential use of pharmacologically modulated HSCs for allogeneic HSCT treatment of rare genetic disorders. The company is planning to evaluate ProHema in an initial clinical trial of pediatric patients with demyelinating lysosomal storage disorders (LSDs). Also, an active research program is being undertaken to develop a second generation HSC therapeutic, which will be specifically designed to enhance the homing of HSCs to the central nervous system (CNS), in order to enhance delivery of essential enzymes to patients with deficiencies.

LSD consultants intrigued by ProHema approach: Our three LSD consultants had positive views on the theoretical potential for pharmacologic modulation in the setting of allogeneic HSCT for LSDs. One of our experts called ProHema *"a very good idea"* and felt that it may be relevant in LSD treatment, as *"it does work in the setting of regular homing to bone marrow…and the niche in CNS resembles the niche in bone marrow."* Our second expert agreed on the rationale of ProHema in this setting, and felt that it was a *"step in the right direction, as one of the goals of transplant is homing into the brain"* for LSDs. At the same time, while this expert noted the early ProHema data to be promising, he was also clear that *"the acceleration of engraftment was not a home run,"* referring to the Phase I trial result. He desired to see an improvement of 7 to 10 days. Our third expert agreed that the improvement in hematopoietic recovery thus far of around 3-4 days may not in and of itself be game-changing, but he was more excited about seeing a potential increase in CNS homing, which "*may open transplant up to diseases which we are not currently transplanting"* and *"could be a big deal."*

Wnt7a analog work is very early, but we believe it has the most upside potential. Fate is also using its understanding of stem cell biology to develop *in vivo* modulators of muscle satellite stem cells (SSCs). Specifically, preclinical experiments have shown that administration of a recombinant Wnt7a protein can lead to expansion of SSCs and improve the regenerative capacity of muscle. These results have obvious implications for and potential in the treatment of muscular dystrophies. Fate is planning to select a Wnt7a drug candidate in 4Q13 and to initiate clinical development in DMD in 2015. With the obvious caveat that this work is still in its very early stages, a quick look at the valuations of companies working in DMD highlights to us the commercial potential and investor interest in the space.

DMD consultant excited about Wnt7a program: Our consultant, a neurologist and neuroscientist specializing in genetic muscle disorders at a major academic medical institution, was *"optimistic"* about Wnt7a-based therapy and felt that *"it is possible it will work"* in DMD. Our expert indicated that Wnt signaling has an important role in muscle stem cell proliferation and considered the rationale of this therapy to be solid, since *"a lot of the problem in DMD is lack of muscle regeneration."* Our expert pointed out the very early nature of the preclinical data which have been produced to date, and emphasized the long path from this stage to advanced clinical development and potential approval. She described the data as *"encouraging"* and remarked that the results to date *"very convincingly"* demonstrate increase in muscle mass, force, and histopathology as a result of Wnt7a administration in the mouse model.

Valuation

To value Fate shares, we use a sum-of-the-parts methodology and estimate the probability-adjusted NPV of: **1)** ProHema sales, royalties, and milestone payments, **2)** Fate's stem cell modulation technology platform, and **3)** the company's current net cash position.

1) ProHema commercialization, royalties, and milestone payments *($10.32/share*): For modeling purposes and in our valuation calculation, we have assumed that the company will partner ex-US rights to this program with a larger biopharma that will market it ex-US, with Fate marketing it in the US on its own by building a specialty sales force. We have assumed that Fate will receive 18%-23% royalties on ex-US sales. We also assume that a partner will pay $50M as an upfront payment in 2015, $30M in 2018 for positive Phase III data and MAA submission, $25M in 2020 for EU approval, and $20M each in 2021, 2023, and 2025 as commercial milestones.

ProHema launches and peak sales: We have modeled that ProHema will be launched in the US and EU in 2019 and 2020, respectively. We estimate that ProHema could reach peak sales in the US and EU of approximately $230M and $290M, respectively, for total US/EU peak sales of around $515M in 2030. Based on these assumptions, and assuming success of the Phase II and Phase III trials, Fate could start recording revenues on ProHema sales in 2019, which could reach a peak of around $295M by 2030.

Discount Rate and Probability of Success (POS): In calculating the net present value of ProHema's free cash flows, we use a 10% discount rate and probability-adjust the revenues to Fate by assigning a 33% overall probability of success (POS) that the compound is successfully developed. We assume a 50% POS for the Phase II trial of ProHema and a 67% POS for the Phase III trial, approval, and market launches in the US and EU, respectively. Using these assumptions, as shown in the table below, we arrive at a probability-adjusted NPV for ProHema of $10.32/share.

ProHema in Hematology– NPV Analysis

($MM)	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ProHema Sales																		
Total US Sales	-	-	-	-	-	-	26.4	53.7	87.2	120.7	135.6	145.0	156.6	169.0	182.4	196.9	212.5	229.4
Total EU Sales	-	-	-	-	-	-	-	38.2	76.9	124.0	170.3	189.9	203.4	217.8	233.3	249.9	267.6	286.7
Total US/EU sales	**-**	**-**	**-**	**-**	**-**	**-**	**26.4**	**91.8**	**164.1**	**244.7**	**305.9**	**334.9**	**359.9**	**386.8**	**415.7**	**446.8**	**480.2**	**516.1**
ProHema Revenues to FATE																		
Total US Sales ($MM)	-	-	-	-	-	-	26.4	53.7	87.2	120.7	135.6	145.0	156.6	169.0	182.4	196.9	212.5	229.4
Total EU royalties ($MM)	-	-	-	-	-	-	-	6.9	14.6	24.8	35.8	41.8	44.7	47.9	53.7	57.5	61.6	65.9
Total Revenue to FATE ($MM)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**26.4**	**60.5**	**101.9**	**145.5**	**171.4**	**186.8**	**201.3**	**216.9**	**236.1**	**254.4**	**274.1**	**295.3**
Milestone payments received from partner			50			30.0	-	25.0	20.0	-	20.0	-	20.0	-	-	-	-	-
COGS	-	-	-	-	-	-	4.0	8.1	13.1	18.1	20.3	21.8	23.5	25.3	27.4	29.5	31.9	34.4
Less royalties paid to Institutions	-	-	-	-	-	-	1.3	3.0	5.1	7.3	8.6	9.3	10.1	10.8	11.8	12.7	13.7	14.8
R&D	-	12.2	13.0	13.3	13.3	13.3	-	-	-	-	-	-	-	-	-	-	-	-
SG&A		4.9	5.2	4.4	3.6	18.8	19.0	20.1	20.5	20.8	21.1	21.5	21.8	22.2	22.5	22.9	23.3	23.7
Tax adjusted EBIT	-	(17.1)	31.8	(17.7)	(16.9)	(2.1)	2.2	51.6	77.4	87.4	123.0	114.1	136.1	123.7	127.3	136.2	147.8	160.2
Tax rate		*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*7%*	*12%*	*13%*	*15%*	*18%*	*22%*	*27%*	*28%*	*28%*	*28%*
ProHema free cash flow	**0.0**	**(17.1)**	**31.8**	**(17.7)**	**(16.9)**	**(2.1)**	**2.2**	**51.6**	**77.4**	**87.4**	**123.0**	**114.1**	**136.1**	**123.7**	**127.3**	**136.2**	**147.8**	**160.2**
% y/y growth							*-206%*	*2253%*	*50%*	*13%*	*41%*	*-7%*	*19%*	*-9%*	*3%*	*7%*	*8%*	*8%*
Discount Period	*0.18*	*1.18*	*2.18*	*3.18*	*4.18*	*5.18*	*6.18*	*7.18*	*8.18*	*9.18*	*10.18*	*11.18*	*12.18*	*13.18*	*14.18*	*15.18*	*16.18*	*17.18*
Discount Factor	*0.98*	*0.89*	*0.81*	*0.74*	*0.67*	*0.61*	*0.56*	*0.50*	*0.46*	*0.42*	*0.38*	*0.34*	*0.31*	*0.28*	*0.26*	*0.24*	*0.21*	*0.19*
PV of ProHema FCF	**0.0**	**(15.3)**	**25.8**	**(13.1)**	**(11.4)**	**(1.3)**	**1.2**	**26.0**	**35.5**	**36.5**	**46.6**	**39.3**	**42.6**	**35.2**	**33.0**	**32.1**	**31.6**	**31.2**

Discount Rate	10%
Perpetual Growth Rate	0%
Final year FCF	$160
Terminal Value	$1,602
Discount Factor	0.19
Present Value of Terminal Value	**$312**
Present Value of Cash Flows	**$376**
Present Value of Total Cash Flows	**$687**
Fully Diluted Shares Outstanding	22
NPV of ProHema in Hematology	**$30.96**
Probability of Success of Phase II trial	***50%***
Probability of Success of Phase III trial	***67%***
Overall Probability of Success	***33%***
NPV of ProHema in Hematology (probability-adjusted)	**$10.32**

Source: Cowen and Company

2) Platform technology value ($2.25/share): We believe that the market assigns a certain value to the company's technology, know-how, IP, and additional preclinical targets. We also believe that this value A) is very difficult to accurately quantify, and B) could increase or decrease significantly, based on market conditions and the outcome of the clinical programs. For the purpose of valuing the shares at this point, we have decided to assign $50M in value to its stem cell technology platform.

3) Net Cash ($2.47/share): Fate ended 2Q13 with $21.3M in cash. In October 2013, Fate raised $40.4M in net proceeds through its IPO by issuing 7.7M shares at $6/share. We estimate that in 3Q13, the company spent ~$4M in operating expenses, bringing its current proforma cash position to approximately $57.8M. Including the $2.8M loan from Silicon Valley Bank, which we expect will be fully repaid in December 2014, we estimate Fate's current proforma net cash position to be approximately $55M, or ~$2.47 per fully diluted share.

FATE: Sum-of-the-parts analysis

ProHema in Hematology	$10.32
Technology value	$2.25
Net Cash	$2.47
Sum-of-the-parts total value for FATE	**$15.05**

Source: Cowen and Company

ProHema in Hematology Revenue Model

Fate owns WW rights to ProHema: Fate currently owns worldwide development and commercialization rights for ProHema. For modeling purposes and in our valuation calculation, we have assumed that the company will partner ex-US rights to this program with a larger biopharma that will market it ex-US, with Fate marketing it in the US on its own, by building a specialty sales force. As stated in the valuation section, we have assumed that Fate will receive 18%-23% royalties on ex-US sales. We also assume that a partner will pay $50M as an upfront payment in 2015, $30M in 2018 for positive Phase III data and MAA submission, $25M in 2020 for EU approval, and $20M each in 2021, 2023, and 2025 as commercial milestones.

HSCT procedures in the US/EU: According to the recent estimate by the US Department of Health and Human Services (HHS), 17,983 HSCTs were performed in the US in 2011, of which 10,403 (58%) were autologous HSCTs and 7,535 (42%) were allogeneic HSCTs. HSCT procedures are more common in the EU, and according to the recent estimate by the European Group for Blood and Marrow Transplantation (EBMT), 35,660 HSCTs were performed in the EU in 2011, of which 21,111 (59%) were autologous HSCTs and 14,549 (41%) were allogeneic HSCTs. It has been noted that the number of HSCT procedures performed globally has been increasing rapidly. According to the Worldwide Network for Blood & Marrow Transplantation (WBMT), the number of HSCTs worldwide increased from 46,563 in 2006 to 51,536 in 2008, representing a 10% increase over this 3-year period.

In our revenue model, we break down total allogeneic HSCT procedures into three groups, corresponding to different hematopoietic stem cell sources:

1) Umbilical cord blood-derived allogeneic HSCT: According to a number of literature sources, cord blood is the cell source in ~10%-20% of allogeneic HSCT procedures. We have assumed the mid-point (15%) of this range, and we estimate that approximately ~1,200 and ~2,200 allogeneic HSCT procedures will be performed using cord blood as the cell source in the US and EU, respectively, by the time the drug is launched in 2019 and 2020.

2) Bone marrow-derived allogeneic HSCT: According to a number of literature sources, bone marrow is the second leading source of stem cells in HSCT, used for 20%-25% of allogeneic HSCT procedures. Based on a 20% number, we estimate that ~1,600 allogeneic HSCT procedures will be performed using bone marrow as the cell source in the US by the time the drug is launched in 2019, and approximately 2,900 allogeneic HSCT procedures will be performed using bone marrow as the cell source in the EU in 2020, our estimated time of EU launch.

3) Peripheral blood-derived allogeneic HSCT: According to a number of literature sources, the majority (65%-70%) of allogeneic HSCTs are performed using peripheral blood as the cell source. Based on a 65% number, we estimate that 5,250 allogeneic HSCT procedures will be performed using peripheral blood for the cell source in the US by the time the drug is launched

in 2019, and approximately 9,500 allogeneic HSCT procedures will be performed using peripheral blood as the cell source in the EU in 2020, our estimated time of EU launch.

Pricing, penetration rates, and sales: In terms of pricing, we have assumed that ProHema will be launched at an average procedure cost of $82,800. We arrive at that price by beginning with a 2014 launch price per procedure of $75,000 and applying a 2% annual increase through 2018. We have assumed a 25% discount to the US pricing in the EU.

- **Peak penetration in cord blood-derived allogeneic HSCTs**: We assume that the Phase III trial of ProHema will be initiated in 2016, will be successful, and that data will be announced in 2018, leading to ProHema approval in 2019 and 2020 in the US and EU, respectively. We estimate that US/EU ProHema sales could reach ~$175M in 2025, and that at 50% penetration in the US and EU, ProHema could reach peak US/EU sales of $250M in 2030.

- **Peak penetration in bone marrow- and peripheral blood-derived allogeneic HSCTs**: Our consultants believe that, once approved for use in allogeneic HSCTs with cord blood, ProHema may also have applicability in procedures using bone marrow and peripheral blood sources. In our model, we have assumed that ~14% of bone marrow-derived and 8% of peripheral blood-derived allogeneic HSCT procedures will be performed using ProHema. We estimate that at 14% penetration in bone marrow-derived allogeneic HSCTs, ProHema could generate peak US/EU sales of ~$90M in 2030. At 8% penetration in peripheral blood-derived allogeneic HSCTs, ProHema could generate peak US/EU sales of ~$170M in 2030.

US/EU peak sales: Using the assumptions outlined above, which translate in a penetration rate for ProHema of 16% in the overall allogeneic HSCT market, result in US/EU sales of ProHema for use in allogeneic HSCT procedures could top $360M in 2025, and could reach peak US/EU sales of ~$515M in 2030.

ProHema Hematology HSCT Revenue Model ($MM)

US ProHema Revenue Model	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US population	319,455,250	322,266,457	325,102,401	327,963,303	330,849,380	333,760,854	336,697,950	339,660,892	342,649,907	345,665,227	348,707,081	351,775,703	354,871,329	357,994,197	361,144,546	364,322,618	367,528,657	370,762,909
Population growth	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*	*0.88%*
# of HSCT performed in the US	18,255	18,416	18,578	18,741	18,906	19,073	19,240	19,410	19,581	19,753	19,927	20,102	20,279	20,457	20,637	20,819	21,002	21,187
# of autologous HSCT	10,587	10,680	10,774	10,869	10,965	11,061	11,158	11,257	11,356	11,456	11,556	11,658	11,761	11,864	11,969	12,074	12,180	12,287
% of autologous HSCT	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*	*58%*
# of allogeneic HSCT	**7,668**	**7,736**	**7,804**	**7,872**	**7,942**	**8,012**	**8,082**	**8,153**	**8,225**	**8,297**	**8,370**	**8,444**	**8,518**	**8,593**	**8,669**	**8,745**	**8,822**	**8,900**
% of allogeneic HSCT	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*	*42%*
% of cord blood derived HSCT	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
# of cord blood derived HSCT	1,150	1,160	1,171	1,181	1,191	1,202	1,212	1,223	1,234	1,245	1,256	1,267	1,278	1,289	1,300	1,312	1,323	1,335
% of cord blood derived HSCT performed with ProHema							*18%*	*29%*	*38%*	*45%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of cord blood derived HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**218**	**355**	**469**	**560**	**628**	**633**	**639**	**644**	**650**	**656**	**662**	**667**
% of bone marrow derived HSCT	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*
# of bone marrow derived HSCT	1,534	1,547	1,561	1,574	1,588	1,602	1,616	1,631	1,645	1,659	1,674	1,689	1,704	1,719	1,734	1,749	1,764	1,780
% of bone marrow derived HSCT performed with ProHema							*3%*	*6%*	*9%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*
# of bone marrow derived HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**48**	**98**	**148**	**232**	**234**	**236**	**239**	**241**	**243**	**245**	**247**	**249**
% of peripheral blood derived HSCT	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
# of peripheral blood derived HSCT	4,984	5,028	5,072	5,117	5,162	5,208	5,253	5,300	5,346	5,393	5,441	5,489	5,537	5,586	5,635	5,684	5,734	5,785
% of peripheral blood derived HSCT performed with ProHema							*1%*	*3%*	*6%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
# of peripheral blood derived HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**53**	**159**	**321**	**431**	**435**	**439**	**443**	**447**	**451**	**455**	**459**	**463**
# of allogeneic HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**319**	**611**	**938**	**1,224**	**1,297**	**1,309**	**1,320**	**1,332**	**1,344**	**1,356**	**1,367**	**1,379**
% penetration in allogeneic HSCT							*4%*	*8%*	*11%*	*15%*	*16%*	*16%*	*16%*	*16%*	*16%*	*16%*	*16%*	*16%*
Price per procedure		$75,000	$76,500	$78,030	$79,591	$81,182	$82,806	$87,774	$93,041	$98,623	$104,541	$110,813	$118,570	$126,870	$135,751	$145,253	$155,421	$166,301
% price increase		*2%*	*2%*	*2%*	*2%*	*2%*	*6%*	*6%*	*6%*	*6%*	*6%*	*7%*	*7%*	*7%*	*7%*	*7%*	*7%*	*7%*
Total US Sales ($MM)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$26**	**$54**	**$87**	**$121**	**$136**	**$145**	**$157**	**$169**	**$182**	**$197**	**$213**	**$229**

EU ProHema Revenue Model	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
EU population	504,393,906	504,898,300	505,403,198	505,908,601	506,414,510	506,920,925	507,427,845	507,935,273	508,443,209	508,951,652	509,460,603	509,970,064	510,480,034	510,990,514	511,501,505	512,013,006	512,525,019	513,037,544
Population growth	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*	*0.10%*
# of HSCT performed in the EU	35,731	35,767	35,803	35,839	35,874	35,910	35,946	35,982	36,018	36,054	36,090	36,126	36,162	36,199	36,235	36,271	36,307	36,344
% of autologous HSCT	21,153	21,174	21,196	21,217	21,238	21,259	21,280	21,302	21,323	21,344	21,366	21,387	21,408	21,430	21,451	21,473	21,494	21,516
# of autologous HSCT	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*	*59%*
# of allogeneic HSCT	**14,578**	**14,593**	**14,607**	**14,622**	**14,637**	**14,651**	**14,666**	**14,680**	**14,695**	**14,710**	**14,725**	**14,739**	**14,754**	**14,769**	**14,784**	**14,798**	**14,813**	**14,828**
% of allogeneic HSCT	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*	*41%*
% of cord blood HSCT	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
# of cord blood HSCT	2,187	2,189	2,191	2,193	2,195	2,198	2,200	2,202	2,204	2,206	2,209	2,211	2,213	2,215	2,218	2,220	2,222	2,224
% of cord blood HSCT performed with ProHema								*18%*	*29%*	*38%*	*45%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of cord blood HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**396**	**639**	**838**	**994**	**1,105**	**1,107**	**1,108**	**1,109**	**1,110**	**1,111**	**1,112**
% of bone marrow derived HSCT	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*
# of bone marrow derived HSCT	2,916	2,919	2,921	2,924	2,927	2,930	2,933	2,936	2,939	2,942	2,945	2,948	2,951	2,954	2,957	2,960	2,963	2,966
% of bone marrow derived HSCT performed with ProHema								*3%*	*6%*	*9%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*
# of bone marrow derived HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**88**	**176**	**265**	**412**	**413**	**413**	**414**	**414**	**414**	**415**	**415**
% of peripheral blood derived HSCT	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
# of peripheral blood derived HSCT	9,476	9,485	9,495	9,504	9,514	9,523	9,533	9,542	9,552	9,561	9,571	9,581	9,590	9,600	9,609	9,619	9,629	9,638
% of peripheral blood derived HSCT performed with ProHema								*1%*	*3%*	*6%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
# of peripheral blood derived HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**95**	**287**	**574**	**766**	**766**	**767**	**768**	**769**	**770**	**770**	**771**
# of allogeneic HSCT performed with ProHema	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**580**	**1,102**	**1,677**	**2,172**	**2,285**	**2,287**	**2,289**	**2,291**	**2,294**	**2,296**	**2,298**
% penetration in allogeneic HSCT								*4%*	*8%*	*11%*	*15%*	*16%*	*16%*	*16%*	*16%*	*16%*	*16%*	*16%*
Price per procedure		$56,250	$57,375	$58,523	$59,693	$60,887	$62,105	$65,831	$69,781	$73,968	$78,406	$83,110	$88,928	$95,153	$101,813	$108,940	$116,566	$124,726
% price increase		*2%*	*2%*	*2%*	*2%*	*2%*	*6%*	*6%*	*6%*	*6%*	*6%*	*7%*	*7%*	*7%*	*7%*	*7%*	*7%*	*7%*
Total EU Sales ($MM)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$38**	**$77**	**$124**	**$170**	**$190**	**$203**	**$218**	**$233**	**$250**	**$268**	**$287**
Total US/EU sales ($MM)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$26**	**$92**	**$164**	**$245**	**$306**	**$335**	**$360**	**$387**	**$416**	**$447**	**$480**	**$516**
US Sales ($MM) - Cord blood derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$18**	**$31**	**$44**	**$55**	**$66**	**$70**	**$76**	**$82**	**$88**	**$95**	**$103**	**$111**
EU Sales ($MM) - Cord blood derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$26**	**$45**	**$62**	**$78**	**$92**	**$98**	**$105**	**$113**	**$121**	**$130**	**$139**
Total US/EU Sales ($MM) - Cord blood derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$18**	**$57**	**$88**	**$117**	**$144**	**$162**	**$174**	**$187**	**$201**	**$216**	**$232**	**$250**
US Sales ($MM) - Bone marrow derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$4**	**$9**	**$14**	**$23**	**$25**	**$26**	**$28**	**$31**	**$33**	**$36**	**$38**	**$41**
EU Sales ($MM) - Bone marrow derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$6**	**$12**	**$20**	**$32**	**$34**	**$37**	**$39**	**$42**	**$45**	**$48**	**$52**
Total US/EU Sales ($MM) - Bone marrow derived HSCTs	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$4**	**$14**	**$26**	**$42**	**$57**	**$60**	**$65**	**$70**	**$75**	**$81**	**$87**	**$93**
US Sales ($MM) - Peripheral blood derived HSCT	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$4**	**$14**	**$30**	**$43**	**$46**	**$49**	**$53**	**$57**	**$61**	**$66**	**$71**	**$77**
EU Sales ($MM) - Peripheral blood derived HSCT	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$6**	**$20**	**$42**	**$60**	**$64**	**$68**	**$73**	**$78**	**$84**	**$90**	**$96**
Total US/EU Sales ($MM) - Peripheral blood derived HSCT	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$4**	**$20**	**$50**	**$85**	**$106**	**$112**	**$121**	**$130**	**$139**	**$150**	**$161**	**$173**

Source: Cowen and Company

ProHema Commercialization Scenario Analysis

In order to capture a number of potential outcomes for ProHema's commercialization in hematologic malignancies, we ran multiple scenario analyses, evaluating the impact on US and EU sales and the resulting valuation for FATE shares, in our model. The key variable we altered was ProHema's peak penetration in the allogeneic HSCT market for hematologic malignancies. In our base case scenario, which is described in the previous section, ProHema achieves peak penetration of 16% in the allogeneic HSCT market, which results in US/EU sales of $360M in 2025, and peak US/EU sales of $515M in 2030.

We altered both the peak penetrations as well as the trajectory of achieving those penetrations, resulting in a wide range of outcomes for both US/EU sales and the value of the company. For simplicity, we have only looked at the allogeneic HSCT market in the steady state it is today, i.e. we have not increased the use of HSCT significantly. Furthermore, we have kept the number of umbilical cord blood transplants steady and have not increased their numbers, while a number of sources are indicating that they may be growing. Despite this, it is clear that, should ProHema succeed in its clinical development, it could become a very successful commercial product, even by achieving modest market penetration, and without counting on significant overall market or umbilical cord blood segment growth.

ProHema Hematology HSCT Market Penetration Scenario Analysis

Scenario Analysis													FATE Value ($/share)	US sales ($MM)	EU sales ($MM)	US/EU Sales ($MM)
Peak penetration	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E				
2%	0%	1%	1%	1%	2%	2%	2%	2%	2%	2%	2%	2%	$5	$30	$37	$67
5%	1%	2%	3%	3%	4%	4%	5%	5%	5%	5%	5%	5%	$7	$74	$92	$166
10%	2%	3%	4%	5%	7%	8%	10%	10%	10%	10%	10%	10%	$10	$148	$185	$333
16%	**4%**	**8%**	**11%**	**15%**	**16%**	**16%**	**16%**	**16%**	**16%**	**16%**	**16%**	**16%**	**$15**	**$229**	**$287**	**$516**
20%	4%	8%	12%	15%	17%	18%	20%	20%	20%	20%	20%	20%	$18	$296	$370	$666
25%	4%	8%	13%	16%	19%	22%	25%	25%	25%	25%	25%	25%	$21	$370	$462	$832
30%	5%	8%	12%	16%	20%	24%	28%	30%	30%	30%	30%	30%	$24	$444	$555	$999
35%	5%	9%	13%	18%	22%	26%	30%	35%	35%	35%	35%	35%	$27	$518	$647	$1,165
40%	5%	10%	16%	21%	26%	31%	36%	40%	40%	40%	40%	40%	$30	$592	$740	$1,332
50%	6%	13%	18%	24%	29%	36%	41%	46%	50%	50%	50%	50%	$36	$740	$925	$1,665

Source: Cowen and Company

Fate: Income Statement and Balance Sheet

Income statement: Fate went public through an IPO on October 1, 2013. For the FY ending December 31, 2012, Fate reported a net loss of $14.2M, or ($13.06) per share, compared to a loss of $13.4M, or ($16.16), in 2011. Total operating expenses in 2012 were $16.2M, compared to $14.5M in 2011. R&D expenses in 2012 were $12M, compared to $9.9M in 2011, while G&A expenses in 2012 were $4.2M, compared to $4.6M in 2011.

For 1H13, Fate reported a net loss of $9.1M, compared to a net loss of $6M in 1H12. Total operating expenses in 1H13 were $8.4M, compared to $7.4M spent in 1H12. R&D expenses in 1H13 were $5.6M, compared to $5.3M spent in 1H12, while G&A expenses in 1H13 were $2.8M, compared to $2.1M in 1H12.

Balance sheet: Fate ended 2Q13 with $21.3M in cash. In October 2013, Fate raised $40.4M in net proceeds through its IPO by issuing 7.7M shares at $6/share. We estimate that in 3Q13, the company spent ~$4M in operating expenses, bringing its current proforma cash position to approximately $57.8M. Including the $2.8M loan from Silicon Valley Bank, which we expect will be fully repaid in December 2014, we estimate Fate's current proforma net cash position to be approximately $55M, or ~$2.47 per fully diluted share.

Post-IPO share count: As of October 1, 2013, the company had 20.4 common shares, 1.8M options, and 40K warrants outstanding, bringing the fully diluted number of shares to approximately 22.2M.

Fate: Options and warrants outstanding

	# of shares	Exercise Price	Amount received when options/warrants are exercised
Warrants for convertible preferred stock	0.04	$0.00	$0.00
Common stock options (exercise price: $1.46)	1.52	$1.46	$2.22
Common stock options (exercise price: $7.00)	0.25	$7.00	$1.75
Total options/warrants outstanding	**1.80**		**$3.97**

Source: Cowen and Company, SEC filings

Fate: Quarterly P&L ($MM)

($MM)	2011A	1H12A	2012A	1H13A	Q3:13E	Q4:13E	2013E	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E
ProHema Revenues to FATE													
Total US Sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total EU royalties	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total ProHema revenues to FATE	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Collaboration revenue	0.8	0.9	1.3	0.4	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0
Grant revenue	0.3	0.6	1.4	0.3	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0
Milestone/License fee	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0
Total revenue	**1.2**	**1.5**	**2.7**	**0.8**	**0.0**	**0.0**	**0.8**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**50.0**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**9.9**	**5.3**	**12.0**	**5.6**	**2.2**	**3.8**	**11.6**	**5.4**	**5.7**	**5.8**	**5.7**	**22.6**	**26.5**
SG&A	**4.6**	**2.1**	**4.2**	**2.8**	**1.8**	**2.2**	**6.8**	**2.0**	**2.1**	**2.0**	**2.0**	**8.1**	**8.7**
Total operating expenses	**14.5**	**7.4**	**16.2**	**8.4**	**4.0**	**6.0**	**18.4**	**7.4**	**7.8**	**7.8**	**7.7**	**30.7**	**35.2**
Operating Income/Loss	**(13.3)**	**(5.9)**	**(13.6)**	**(7.6)**	**(4.0)**	**(6.0)**	**(17.6)**	**(7.4)**	**(7.8)**	**(7.8)**	**(7.7)**	**(30.7)**	**14.8**
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest expense	(0.1)	(0.2)	(0.5)	(0.2)	(0.1)	(0.1)	(0.4)	(0.1)	(0.1)	(0.1)	(0.1)	(0.4)	0.0
Other income (expense)	(0.0)	0.1	(0.2)	(1.3)	(1.0)	0.0	(2.3)	0.0	0.0	0.0	0.0	0.0	0.0
Pretax income	(13.4)	(6.0)	(14.2)	(9.1)	(5.1)	(6.1)	(20.3)	(7.5)	(7.9)	(7.9)	(7.8)	(31.1)	14.8
Income tax expense	0.0		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net loss attributable to common stock	**(13.4)**	**(6.0)**	**(14.2)**	**(9.1)**	**(5.1)**	**(6.1)**	**(20.3)**	**(7.5)**	**(7.9)**	**(7.9)**	**(7.8)**	**(31.1)**	**14.8**
EPS (basic)	**($16.16)**	**($5.96)**	**($13.06)**	**($7.41)**	**($0.41)**	**($0.30)**	**($1.78)**	**($0.36)**	**($0.38)**	**($0.38)**	**($0.37)**	**($1.49)**	**$0.44**
EPS (diluted)	**($16.16)**	**($5.96)**	**($13.06)**	**($7.41)**	**($0.41)**	**($0.30)**	**($1.78)**	**($0.36)**	**($0.38)**	**($0.38)**	**($0.37)**	**($1.49)**	**$0.41**
Basic shares	0.8	1.0	1.1	1.23	12.5	20.4	11.4	20.6	20.8	21.0	21.2	20.9	34.0
Diluted shares	0.8	1.0	1.1	1.23	14.3	22.2	12.6	22.4	22.6	22.9	23.1	22.8	35.9

Source: Cowen and Company, SEC Filings

Fate: Annual P&L ($MM)

($MM)	2011A	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ProHema Revenues to FATE																				
Total US Sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	26.4	53.7	87.2	120.7	135.6	145.0	156.6	169.0	182.4	196.9	212.5	229.4
Total EU royalties	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.9	14.6	24.8	35.8	41.8	44.7	47.9	53.7	57.5	61.6	65.9
Total ProHema revenues to FATE	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**26.4**	**60.5**	**101.9**	**145.5**	**171.4**	**186.8**	**201.3**	**216.9**	**236.1**	**254.4**	**274.1**	**295.3**
Collaboration revenue	0.8	1.3	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Grant revenue	0.3	1.4	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Milestone/License fee	0.0	0.0	0.0	0.0	50.0	0.0	0.0	30.0	0.0	25.0	20.0	0.0	20.0	0.0	20.0	0.0	0.0	0.0	0.0	0.0
Total revenue	**1.2**	**2.7**	**0.8**	**0.0**	**50.0**	**0.0**	**0.0**	**30.0**	**26.4**	**85.5**	**121.9**	**145.5**	**191.4**	**186.8**	**221.3**	**216.9**	**236.1**	**254.4**	**274.1**	**295.3**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**5.3**	**11.1**	**18.2**	**25.4**	**28.9**	**31.1**	**33.5**	**36.2**	**39.2**	**42.3**	**45.6**	**49.2**
R&D	**9.9**	**12.0**	**11.6**	**22.6**	**26.5**	**34.5**	**39.7**	**41.0**	**41.9**	**42.9**	**46.8**	**52.9**	**63.2**	**62.4**	**71.7**	**71.1**	**75.5**	**82.9**	**89.4**	**94.9**
SG&A	**4.6**	**4.2**	**6.8**	**8.1**	**8.7**	**8.9**	**9.1**	**25.2**	**25.5**	**26.9**	**27.3**	**27.8**	**28.3**	**28.8**	**29.2**	**29.8**	**30.3**	**30.8**	**31.3**	**31.9**
Total operating expenses	**14.5**	**16.2**	**18.4**	**30.7**	**35.2**	**43.4**	**48.8**	**66.2**	**72.8**	**80.9**	**92.3**	**106.1**	**120.4**	**122.3**	**134.5**	**137.0**	**144.9**	**156.0**	**166.3**	**176.0**
Operating Income/Loss	**(13.3)**	**(13.6)**	**(17.6)**	**(30.7)**	**14.8**	**(43.4)**	**(48.8)**	**(36.2)**	**(46.3)**	**4.7**	**29.6**	**39.4**	**71.0**	**64.5**	**86.8**	**79.9**	**91.1**	**98.4**	**107.8**	**119.4**
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest expense	(0.1)	(0.5)	(0.4)	(0.4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other income (expense)	(0.0)	(0.2)	(2.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pretax income	(13.4)	(14.2)	(20.3)	(31.1)	14.8	(43.4)	(48.8)	(36.2)	(46.3)	4.7	29.6	39.4	71.0	64.5	86.8	79.9	91.1	98.4	107.8	119.4
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	2.1	4.7	9.2	9.7	15.6	17.6	24.6	27.6	30.2	33.4
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*7%*	*12%*	*13%*	*15%*	*18%*	*22%*	*27%*	*28%*	*28%*	*28%*
Net loss attributable to common stock	**(13.4)**	**(14.2)**	**(20.3)**	**(31.1)**	**14.8**	**(43.4)**	**(48.8)**	**(36.2)**	**(46.3)**	**4.4**	**27.5**	**34.7**	**61.8**	**54.8**	**71.1**	**62.3**	**66.5**	**70.8**	**77.6**	**85.9**
EPS (basic)	**($16.16)**	**($13.06)**	**($1.78)**	**($1.49)**	**$0.44**	**($1.23)**	**($1.33)**	**($0.95)**	**($1.17)**	**$0.11**	**$0.64**	**$0.78**	**$1.33**	**$1.13**	**$1.41**	**$1.19**	**$1.22**	**$1.25**	**$1.32**	**$1.40**
EPS (diluted)	**($16.16)**	**($13.06)**	**($1.78)**	**($1.49)**	**$0.41**	**($1.23)**	**($1.33)**	**($0.95)**	**($1.17)**	**$0.10**	**$0.61**	**$0.73**	**$1.26**	**$1.07**	**$1.34**	**$1.13**	**$1.16**	**$1.18**	**$1.25**	**$1.33**
Basic shares	0.8	1.1	11.4	20.9	34.0	35.3	36.8	38.2	39.8	41.3	43.0	44.7	46.5	48.4	50.3	52.3	54.4	56.6	58.8	61.2
Diluted shares	0.8	1.1	12.6	22.8	35.9	37.4	38.9	40.4	42.0	43.7	45.5	47.3	49.2	51.1	53.2	55.3	57.5	59.8	62.2	64.7

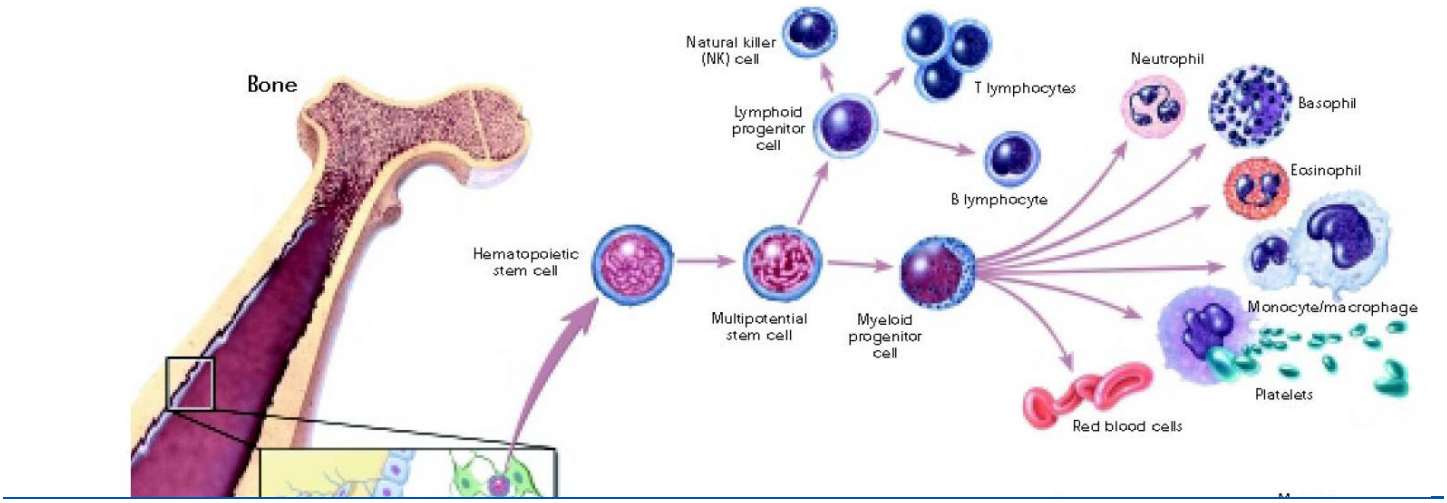
Source: Cowen and Company, SEC Filings

Hematopoietic Stem Cell (HSC) Modulation: ProHema

Stem cells are cells which have potential to generate many different cell types. They are broadly categorized as **embryonic** stem cells (*cells derived from embryos)* and **adult** stem cells *(non-embryonic)*. There are three general characteristics of stem cells, which distinguish them from other cell types: **1)** proliferative capacity, with division, replication, and renewal of cells over long periods; **2)** unspecialized status, without tissue-specific structures, and **3)** ability to form specialized cells, in a process known as *differentiation*. Adult stem cells typically develop into cell types which are characteristic of the tissue in which they are located (examples include bone marrow, muscle, brain). These stem cells produce replacements for cells which are lost through normal aging, injury, or disease.

All mature blood cells derive from hematopoietic stem cells (HSCs). HSCs are immature, pluripotent, progenitor cells which develop into all blood cell types, including white blood cells (WBCs, such as lymphocytes, neutrophils, monocytes), red blood cells (RBCs), and platelets. HSCs have been used for the treatment of malignant and non-malignant diseases in order to replace an individual's hematopoietic system, in a procedure known as hematopoietic stem cell transplant (HSCT). HSCs are found in and can be collected from: **1)** bone marrow, **2)** peripheral blood, and **3)** umbilical cord blood (collected following birth of an infant).

HSC Differentiation and Blood Cell Development

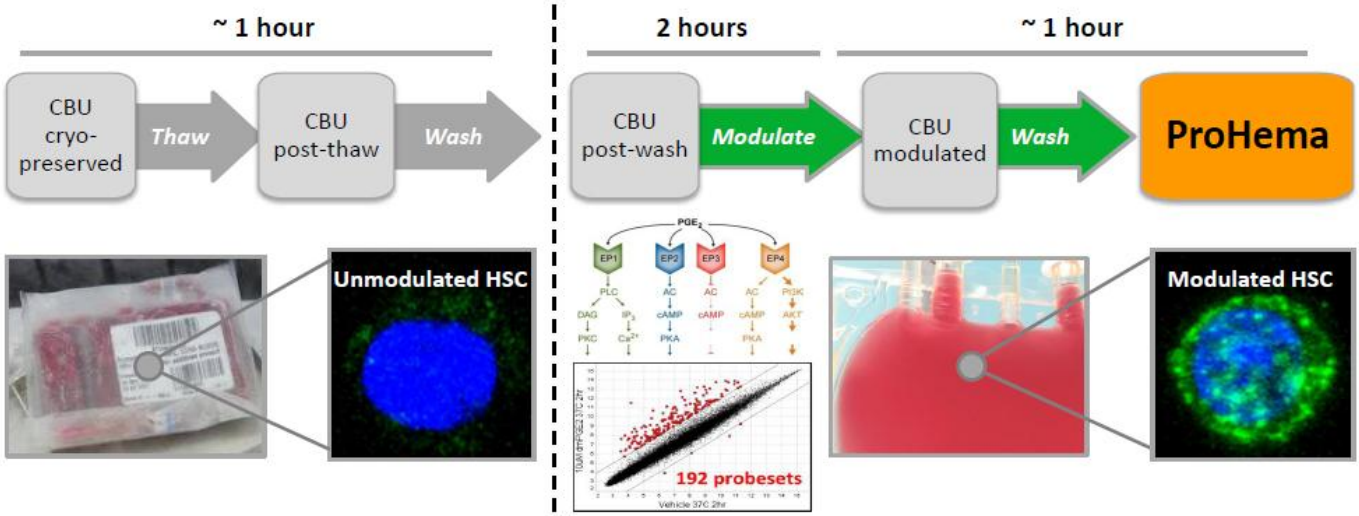


Source: NIH

ProHema (formally called ProHema-CB Suspension for Infusion), is a pharmacologically-modulated HSC therapeutic derived from umbilical cord blood, composed of human cord blood cells, in which there has been optimization of HSCs *ex vivo* using a small molecule. This therapeutic is meant for use in HSCT. The modulator, FT1050 (dmPGE2, 16,16-dimethyl prostaglandin E2), improves the cell surface expression of key *homing* proteins. This improves **engraftment**, *(the localization and integration of HSCs within a targeted tissue, where they can produce new cells).* ProHema is produced from the treatment of cryopreserved, human

umbilical cord blood units (CBUs) with FT1050. The CBUs are identified through online search facilities from global cord blood banks. FT1050 is sourced from a third-party manufacturer. The 2-hour modulation process is performed on-site, at the center of care on the day of transplant, and requires no new processing systems. The CBUs do not leave the clinical center. Post modulation, a wash is performed to remove any residual FT1050. ProHema is a biologic and regulated as a cell therapy by FDA (CBER, Center for Biologics Evaluation and Research).

ProHema Production

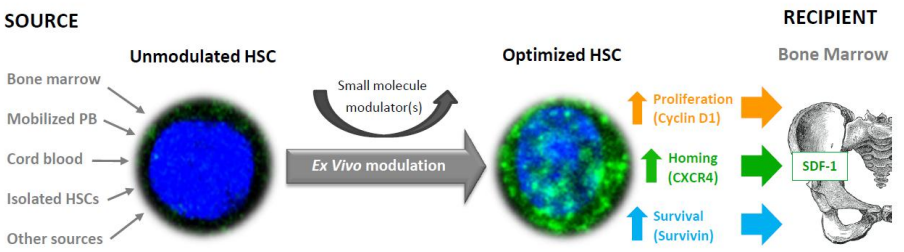


Source: Fate Therapeutics Presentation

The principle behind ProHema is that *ex vivo* modulation of HSCs can optimize their biologic properties *in vivo*. This is a broader HSC modulation platform idea, of which ProHema is one (and the lead) example. Through pharmacologic modulation, upregulation of genes involved in cell proliferation (e.g., CyclinD1), survival (e.g., Survivin), and homing (e.g., CXCR4) may improve engraftment and other clinical outcomes.

Fate has conducted preclinical and clinical work thus far using ProHema on umbilical cord-derived blood. The company believes that Fate's ProHema platform may eventually be applied independently of stem cell source (i.e., not only using umbilical cord blood-derived, but also bone marrow-derived and peripheral blood-derived) and HSCT settings (i.e., also autologous).

HSC Modulation Platform



Source: Fate Therapeutics Presentation

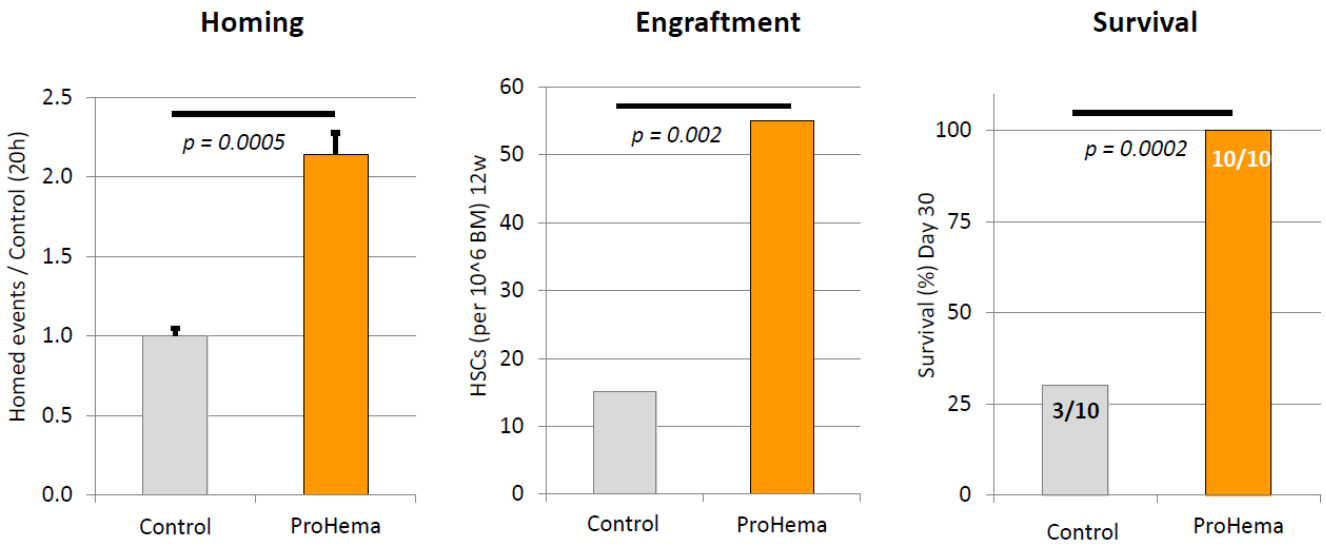
ProHema: Preclinical Studies

In preclinical studies, *ex vivo* modulated human HSCs were evaluated in a mouse model of HSCT. Results were published in 2009 (Hoggatt J et al., *Blood* 2009). HSCs were derived from human umbilical cord blood. Cells were incubated with dmPGE2 for 2 hours. In the animal HSCT model, mice were irradiated and then transplanted with either dmPGE2-treated or vehicle-treated cells. Recipient bone marrow was then evaluated.

Homing of HSCs was assessed by labeling of cells with carboxyfluorescein (CFSE) before treatment. Cells treated with dmPGE2 increased efficiency of homing to the bone marrow niche by 2-fold compared to vehicle-treated (control) cells (p=0.0005). At 12 weeks after transplantation, there was a significant, approximately 4-fold increase in HSC engraftment with dmPGE2-treated cells compared to control cells (p=0.002). This increase was maintained throughout 20 weeks after transplantation.

In another series of mouse HSCT experiments, survival was evaluated following transplants with limited HSC dose. During the 30-day observation period, 7 out of 10 irradiated mice in the control group died as a result of the suboptimal transplanted cell dose. However, there was 100% survival for the mice receiving dmPGE2-treated cells (p=0.0002 vs. control).

Preclinical Studies: Effects on Homing, Engraftment, and Survival



2-fold increase in homing of HSCs to the bone marrow niche

4-fold increase in long-term HSC engraftment

Improved survival of mice transplanted with limited cell dose

Source: Fate Therapeutics Presentation, Fate S-1

ProHema: Clinical Development

ProHema-01: Phase Ib Clinical Proof-of-Concept Trial

- *Trial started: August 2010*
- *Trial completed: September 2011*
- *Results published: Blood 2013*

Trial Design: This was a clinical proof-of-concept, Phase Ib trial of ProHema, which evaluated adult patients with hematologic malignancies undergoing allogeneic HSCT with double umbilical cord blood transplant (UCBT) after a reduced-intensity conditioning (RIC) regimen. Patients had diagnoses of acute leukemia, non-Hodgkin's lymphoma, and myelodysplastic syndrome. There were 12 patients, with median age 57.5 years, who received ProHema and an unmanipulated cord blood unit (CBU). The trial was conducted at the Dana Farber Cancer Institute and the Massachusetts General Hospital at Harvard Medical School. Results were compared against a historical control cohort of 53 patients with hematologic malignancies who had received double UCBT and had been previously at these institutions.

Study Endpoints: The primary endpoint of the trial was safety. Secondary endpoints included assessment of time to engraftment and 100-day survival.

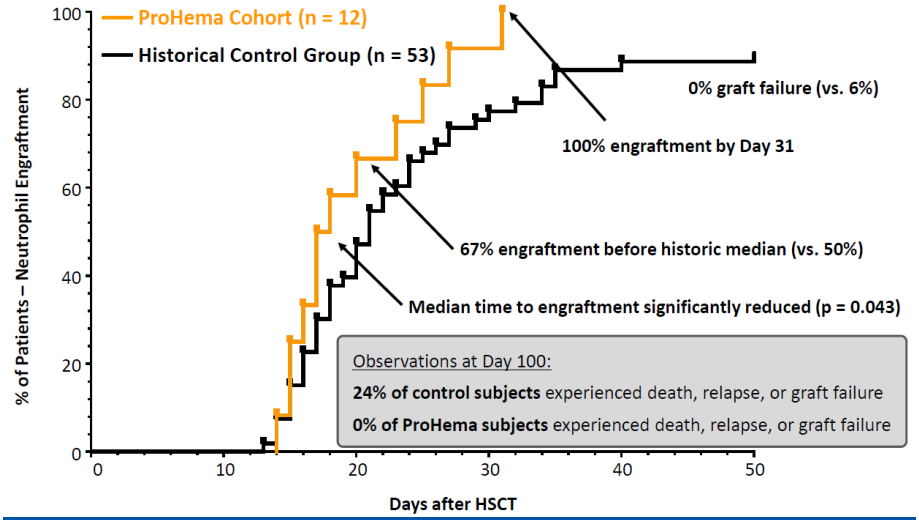
Study Results: Results of the Phase Ib trial were published in 2013 (Cutler C et al., *Blood* 2013). The majority of UCB units were 4/6 HLA-matched to each other and to the recipient, and cell doses between units were similar. Each UCB unit was required to have ≥1.5 x 10^7 total nucleated cells/kg, and the combined cell dose was required to be ≥ 3.7 x 10^7 total nucleated cells/kg. The ProHema modulation process did not cause significant cell loss, with an average 90% viable cell recovery.

Neutrophil and Platelet Engraftment: There was a statistically significant reduction of 3.5 days in the median time to neutrophil engraftment in the ProHema cohort (17.5 days, range 14-31 days, n=12) compared to historical control (21 days, n=53), p=0.045. Neutrophil engraftment was defined as peripheral blood neutrophil count ≥ 500 cells/mcL for three consecutive days. In the ProHema cohort, there was a 0% non-engraftment rate at Day 35, and there was a 0% graft failure rate. The median time to platelet engraftment was 43 days (range, 26-60 days), and by Day 60, 11/12 patients had engrafted platelets. Platelet engraftment was defined as platelet count of 20 x 10^9 cells/L, without transfusion support, for three days.

Survival and Chimerism Assessment: The 100-day survival rate was 100% for the ProHema group, compared with 87% for the historical control. At Day 100, there was 0% failure (death, relapse, or graft failure) in the ProHema cohort vs. 24% failure for the historical control cohort. By Day 100, the incidence of Grade II-IV acute graft-versus-host disease (GVHD) was 8% in ProHema patients, compared to 17% in the historical control. A chimerism assessment was also conducted to determine which of the two CBUs contributed to long-term hematopoietic restoration. Donor chimerism was assessed from peripheral blood mononuclear cells with analyses of short tandem repeat loci. At Day 100, 83% (10/12) of the ProHema patients had early and sustained engraftment of the ProHema unit, which contributed 100% to hematopoiesis.

At a median follow-up of 24.6 months, the 1-year and 2-year PFS rates in the ProHema cohort were 62% and 31%, respectively. The 1-year and 2-year OS rates were 75% and 39%, respectively. Causes of death in 8 patients included relapse (n=3), treatment-related complications (n=4), and suicide (n=1).

Phase Ib Trial: Neutrophil Engraftment



Source: Fate Therapeutics Presentation

Safety Data: ProHema was well tolerated. The AEs related to ProHema included Grade 1-2 infusion-related events in four patients, including chills, flushing, abdominal pain, and cough. One additional patient with known coronary artery disease had transient Grade 4 ST elevation following infusion, with evidence of myocardial ischemia.

FDA End-of-Phase I Meeting: Fate had an End-of-Phase I meeting with the FDA in 1Q12, at which FDA guidance was provided on potential Phase III study endpoints. Fate has reported that the guidance suggested time to engraftment of neutrophils, platelets, or both could be acceptable as a primary endpoint to support approval. Also, it was indicated that a single Phase III trial with both adult and pediatric patients could be sufficient for approval in both groups, depending on results.

ProHema-02: Phase I Trial With Single UCBT in Adults

While this trial is evaluating adults, it is being undertaken as part of the ProHema clinical development plan in the pediatric population with hematologic malignancies, for which the HSCT procedure typically uses a single CBU. This trial, which is evaluating safety in the single UCBT setting, is a first step in exploring the potential of ProHema in pediatric patients.

Trial Design: This is a Phase I trial evaluating ProHema in adult patients with hematologic malignancies who are undergoing single UCBT. Patients receive the same RIC regimen used in the ProHema-01 trial. Post conditioning, they receive a single ProHema CBU. The primary endpoint of the trial is safety. Secondary endpoints include engraftment measures, rates of graft-versus-host disease, relapse rate, and survival.

Preliminary Results: The trial has enrolled 8 patients, with 6 patients (age 19-64 years) evaluable and having the diagnoses of acute myelogenous leukemia (AML, n=4),

myelodysplastic syndrome (MDS, n=1) and multiple myeloma (MM, n=1). There were 4 out of 6 patients who engrafted on Days 17, 19, 22, and 37. Two patients had primary graft failure. There was 100% survival at 100 days (all six patients survived). No cases of acute or chronic GVHD have been observed. AEs were reported to be limited to common transplant-related side effects.

What's Next? ProHema Pediatric Plan

The company has indicated that it has preliminarily discussed with FDA a plan to conduct a Phase Ib trial in children and adolescents (n=12) with hematologic malignancies using a single ProHema unit, reporting that FDA *"was open to our conducting such a pediatric trial."* Pending final approval of the trial protocol by FDA, Fate plans to initiate this Phase Ib trial. The primary endpoint of the trial is anticipated to be safety, defined by neutrophil engraftment. Expected secondary endpoints include time to neutrophil engraftment, cumulative incidence of neutrophil engraftment by Day 42, time to platelet engraftment, cumulative incidence of platelet engraftment by Day 180, graft failure rate, GVHD rate, OS, and event-free survival.

The company plans to conduct the trial at 1-3 US clinical centers and anticipates initiation of enrollment in mid-2014. Management has indicated its view that this trial may be conducted under the current ProHema IND (amending the existing IND). However, the company has stated that the FDA may require a new IND upon review of the ProHema clinical development plan in pediatric patients.

ProHema Formulation Change and August 2013 IND Amendment

During 2Q13, Fate completed additional preclinical studies using an enhanced ProHema formulation which uses nutrient-rich media (NRM) during the modulation process. The company refers to this new ProHema formulation as the **NRM formulation**. The new media incorporates a stabilizing agent which prevents cells from lysing, improving product viability and potency. In the ProHema-01 trial, the manufacture of ProHema used standard processing media, which, according to the company, was the same as that commonly used in present clinical settings for thawing and washing of umbilical CBUs. In 2Q13, the company paused enrollment in the ongoing Phase II ProHema-03 trial, discussed below, in order to incorporate the NRM formulation.

Preclinical Studies: In *in vitro* studies, including a transwell migration assay, it was demonstrated that use of the NRM formulation improved HSC viability, as measured by HSC recovery, which was 107% compared to 88% with the prior media. The HSC population more than doubled, from 62% to 131%, with the NRM formulation. Homing potential of HSCs was also improved with the new formulation, with 34% for NRM vs. 7% with prior media.

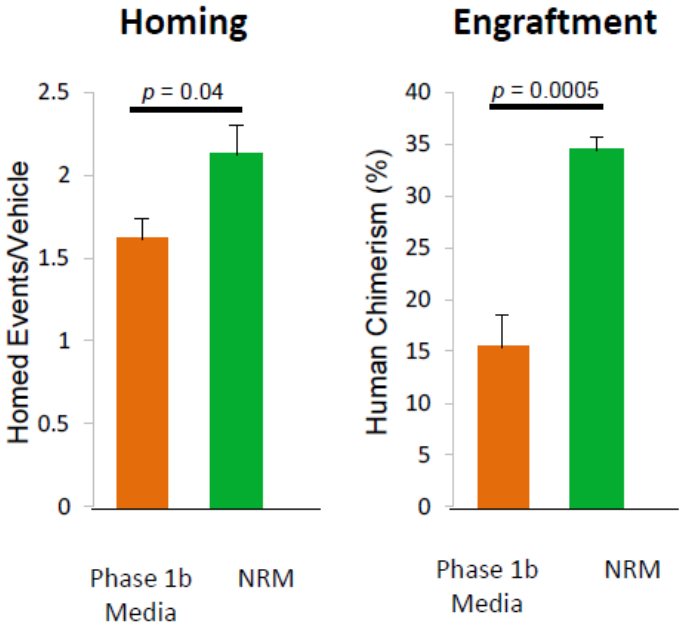
Preclinical *In Vitro* Assay Results with NRM Formulation

Measure of Activity	Prior Media	NRM
Expression of relevant genes	2-6 fold	9-126 fold
Homing potential	7%	34%
Viable HSC recovery	88%	107%
Increase in HSC population	62%	131%

Source: Cowen and Company, Fate S-1

Preclinical studies were also completed in animal (mouse) HSCT models using the NRM formulation. The NRM formulation was associated with significantly more homing events compared to the prior media (p=0.04). Also, there was more than two-fold improvement in engraftment with NRM (p=0.0005).

Preclinical Mouse Model Results with NRM Formulation



Source: Fate Therapeutics Presentation

IND Amendment: On August 1, 2013, Fate submitted a ProHema IND amendment to FDA. This amendment included preclinical and product development data in support of the NRM formulation, including no additional safety risk with use of the new media. The new media is used in the first wash step and in the incubation with FT1050. It is then washed out in the second wash.

ProHema-03: Phase II Trial of ProHema in Adults With Hematologic Malignancies

- *Trial initiated: December 2012*
- *Enrollment Pause: 2Q13*
- *Protocol amendment: August 2013*
- *Enrollment resumption planned: 1H14*
- *Full data expected: Mid-2015*

Trial Design: This is a randomized, controlled, multicenter, Phase II trial evaluating ProHema in adult patients with hematologic malignancies who are being treated with double UCBT after myeloablative (MAB) conditioning or RIC. Patients will be randomized 2:1 to receive ProHema with an unmanipulated CBU or two unmanipulated CBUs. The trial is expected to enroll 60 patients, with 40 assigned to ProHema and 20 to the control group. Patients will be stratified according to the type of conditioning regimen used (MAB or RIC).

Study Endpoints: The primary endpoint of the trial is the cumulative incidence of neutrophil engraftment by a pre-specified control median, which is adjusted based on median times in the control arm. Secondary endpoints include time to neutrophil engraftment, cumulative incidence of neutrophil engraftment by Day 42, time to platelet engraftment, cumulative incidence of platelet engraftment by Day 180, graft failure rate, GVHD rate, event-free survival, and OS.

Trial Statistics: The trial has 80% power to demonstrate with statistical significance that 70% of ProHema patients have neutrophil engraftment before the control median engraftment time.

Enrollment Pause and Protocol Amendment: In 2Q13, Fate paused enrollment in the Phase II trial, in order to introduce a CMC (Chemistry, Manufacturing, and Controls) modification allowing the manufacture of ProHema with the new NRM formulation. In addition to the IND amendment, an amended protocol for the ProHema-03 trial was submitted in August 2013. The amendment stated that a full cohort of 60 patients will be enrolled under the CMC change to use the new NRM formulation. There will be 10 clinical sites. Patients enrolled prior to the amendment will be followed and analyzed separately.

Study Results in Patients Enrolled Prior to Amendment: There were 11 patients enrolled in the trial at 8 clinical sites before the enrollment pause. All patients had undergone conditioning with a MAB regimen. Eight patients were randomized to ProHema, and three patients were assigned to the control group. The control patients had engraftment on Days 30, 31, and 40, for a control median of 31 days. In the ProHema group, 5 of 8 (63%) patients had engraftment before the control median (on Days 14, 19, 24, 28, 30), and 2 patients engrafted after the control median, on Days 40 and 48. The change in the median time to engraftment with ProHema compared to control was 3 days (28 days vs. 31 days). There was one ProHema patient who had failure of engraftment. At a median follow-up of 156 days, 5/8 ProHema patients survived and had engraftment, compared to 1/3 control patients. There was one ProHema patient with Grade IV acute GVHD, and one patient in the control group with Grade

III acute GVHD. The AEs associated with ProHema were reported as infusion-related side effects.

What's Next? Fate has indicated that, based on communication with FDA, resumption of enrollment in the Phase II ProHema-03 trial is expected in 1H14. Full data are anticipated in mid-2015.

Potential Phase III Program Plan: Fate has indicated that, should the Phase II ProHema-03 trial be successful, additional regulatory guidance would be sought to begin a Phase III registration trial for ProHema. Based on preliminary feedback from FDA, management has guided that the Phase III program may possibly only require a single trial, with both adult and pediatric patients, and an anticipated enrollment of approximately 175-225 patients. This would be a multicenter study, including ~25 to 30 US clinical transplant centers. The Phase III trial would be expected to have 1:1 randomization and be powered for time-to-event analysis. Time to engraftment of neutrophils, platelets, or both is anticipated as an acceptable endpoint to support approval. At this time, the company is projecting a 2H15 timeframe for initiation of the Phase III trial.

The Consultant's Corner: *What Do Our Consultants Think of ProHema?*

We consulted with five hematologist/oncologists specializing in hematopoietic stem cell transplantation at major, leading transplantation centers across the US. This group included specialists in both adult and pediatric stem cell transplantation. All of our consultants had significant clinical practices including allogeneic HSCT and the use of umbilical cord blood as a cell source. Additionally, each of our experts was familiar with ProHema, and some were participants in ProHema clinical trials.

All of our experts indicated that *peripheral blood* is the most common source of HSCs used in allogeneic HSCT today, with umbilical cord blood (UCB) accounting for approximately 10%-20% of procedures in adults and a slightly higher proportion, 20%-30%, in children.

Advantages and disadvantages of UCB as a cell source:

The advantages of UCB were universally acknowledged as:

1) convenience and ease of accessibility,

2) increased flexibility in HLA matching,

3) reliability as an alternative HSC source, allowing expansion of the donor pool and viability of transplant for more patients, especially minorities, and

4) less GVHD complications, likely resulting from the relatively naïve immunity of fetal cells.

Likewise, our experts were aligned on the disadvantages of UCB, including:

1) the relatively limited number of HSCs in a CBU, resulting from the small overall quantity of the blood source,

2) delays in engraftment and hematopoietic recovery,

3) relative immunologic disadvantage and deficiency because of the smaller number of mature cells, and

4) higher risk of early complications, infections, and transplant-related morbidity.

With regard to the growth of UCB use in transplantation, the physicians in our group were somewhat mixed, with some noting that it is *"rising dramatically"* and others describing it as *"relatively flat."* They did acknowledge that this could be transplant-center dependent. There was agreement on the relative timing for hematopoietic recovery (time to neutrophil engraftment) related to HSC sources, with peripheral blood having the shortest time (~12-15 days), bone marrow an intermediate time (~15-20 days), and UCB the longest time (~25-30 days) in a standard (MAB) transplant.

Is ProHema easy to use? Our consultants were all familiar with the ProHema data presented to date and understood the ProHema process, with some having direct experience with the product in the trial setting. Our experts were completely aligned on the ease and relative simplicity of the ProHema process. They called the process *"a very minor additional step," "rather straightforward," "a very simple type of technique," "practical, not at all problematic,"* and *"quite an attractive process which is not a big deal."* Indeed, this low impact, non-laborious process appeared to be one of the key attractions to the use of ProHema among our group. These physicians were not concerned about any potential staff training requirements, remarking that *"any lab that is processing cord blood could do this"* and calling additional efforts *"trivial for a good lab staff."* Additionally, one further appeal of the ProHema process voiced by our consultants was the on-site (at the individual transplant center laboratory) modulation, allowing stem cells to remain in the center at all times. As one of the physicians commented, *"it is nerve-wracking to outsource a product…knowing it is in the laboratory and the product is safe--that is worth something--less stress to me and to the patient."*

Does the ProHema approach make sense? With regard to the ProHema data, all of our experts noted the early nature of the results, but did feel that the data were "*interesting*" and *"promising."* In particular, they appeared to be intrigued by the underlying strategy of ProHema modulation for homing enhancement, and differentiated this from other approaches focused on *ex vivo* expansion (discussed later in our report, see "Competitor Agents in Development for CBU Enhancement") of cord blood cells, which were viewed generally as "*laborious,*" "*expensive,*" and "*time-consuming*." As one of our consultants commented, "*we are relying on the cells to eventually find their space; cells will go all over, but we want them in the marrow space."* He felt that it was rational to focus on homing, given that the ProHema approach affects the surface expression of molecules so that HSCs *"will find their way"* compared to interventions focused on cell proliferation *("a cell number issue")*.

What about the data so far? While all our consultants did view the preliminary ProHema data to have potential, the group was split on the strength of the clinical results thus far, in particular regarding the reduction in time to neutrophil engraftment reported in the Phase I trial (compared to historical control). On the one hand, there were a couple physicians who viewed the reduction in engraftment time of 3-4 days as *"clinically meaningful,"* given that the longer amount of time a patient is neutropenic leads to an increased risk of transplant-related morbidity. They felt that this improvement would reduce length of stay in the hospital, leading to relative risk reduction for the patient, as well as potential cost savings (a meaningful economic benefit). On the other hand, there were two physicians in our group who questioned the impact, stating *"I'm not sure if 3 days is overall meaningful"* and asking, *"is it meaningful in terms of death and infections?"* These physicians were focused on long-term results, and expressed some doubt that the time to engraftment result demonstrated thus far would ultimately provide any survival advantage. Both desired to see a faster time to hematopoietic recovery. One expert remarked, *"if you shorten the time by 10 days, then you would see an impact on survival…4 days--no."* Our other consultant in that camp stated, *"the more reduction, the better…even 1 week."* In the middle of our overall group, one expert focused on the median time to engraftment reported (17.5 days), commenting, *"17 days is reasonable, not super-fast."* He pointed out that his threshold for neutropenia is 16 days, feeling that complications and

expense increase dramatically after this time, and cautioned on the importance of examining the *"outliers"* in trials, rather than just the average or median time results.

The use of two CBUs: One particularly notable aspect of the ProHema data indicated by our consultants in the context of double UCBT was the preferential engraftment of the ProHema CBU over the other unmanipulated unit. As our experts pointed out, it is typical in a double UCBT for one unit to ultimately engraft and be the source of hematopoietic recovery. The biologic reasons for this are unclear, and the "winning" unit cannot be predetermined. One of our consultants indicated that the ProHema unit *"earned a competitive advantage because of treatment"* with the modulation and pointed out that the *"ability to push engraftment to the ProHema unit when you put in two units"* is valuable. Another one of our experts remarked that *"if you can predict which cord will engraft, there are lots of other applications."* Our consultant felt this control could be a significant tool and mentioned, as an example, favoring the cord with better HLA match for engraftment in a double UCBT setting.

Will ProHema be approved, and if approved, will it be used? Overall, our consultants felt that there is a *"reasonable"* chance of a successful ProHema clinical trial program and ultimately approval, if meaningful improvements can be demonstrated in hematopoietic recovery. One of our experts remarked that knowing Fate is working with the FDA for design of a trial which will support an approval pathway provides further confidence. In terms of potential uptake of ProHema, if approved, our physicians were aligned in expressing a reasonable chance of adoption as well. Another of our experts commented, *"allogeneic transplant is a growth industry, growing by 10%-15% every year, and the growth is in mismatched transplants."* Thus, he felt that there would be adoption, if ProHema is shown to work. In general, our consultants voiced that, in terms of uptake for this type of product, the transplantation community is seeking **1)** evidence of efficacy (i.e., rapid engraftment), and **2)** ease and convenience. As one of our physicians summarized, *"if you can achieve the same endpoint with a lot less work, that will ultimately win."*

How much could you charge? We asked our consultants about the acceptable incremental cost for a product such as ProHema in allogeneic HSCT. In order to probe on this, we queried specifically, using a theoretical additional cost of $50,000-$75,000. Overall, our group of physicians found this theoretical cost to be rather high, with some expressing more muted concerns and others being more outspoken. Some of our experts focused on the potential cost-effectiveness ProHema might provide in totality, feeling that outcome benefits may offset the incremental cost of the product. As one remarked, *"if the product can shave days off of the hospital admission, the price may be reasonable."* Others in the group described the theoretical cost as *"horribly expensive," "way out of range,"* and *"prohibitive--a turn off."* In particular, they pointed out that the use of double cords already adds at least ~$50,000 due to the cost of obtaining a CBU (estimated to be in the ~$25,000-$40,000 range). Also, they indicated that procedure costs using haploidentical donors, which are becoming more common and considered a competing source to UCB, are much cheaper (discussed later in our report, see "Alternative HSC Source: Haploidentical HSCT").

ProHema use in bone marrow- and peripheral blood-derived cells: Finally, we discussed with our consultants the potential applicability of the ProHema modulation platform in other HSC-sourced allogeneic transplants and in autologous transplantation. All of our consultants agreed theoretically that the modulation process could be applied outside of allogeneic cord blood transplant. However, they all uniformly questioned the amount of potential benefit that might be achieved outside of this indication. As one of the physicians in the group summarized, *"in cord blood, there is latitude to tighten time up,"* but less so with bone marrow and peripheral blood sources. A couple of physicians in the group did think bone marrow transplantation could be a reasonable next target, given its current intermediate engraftment time overall, though another one of our experts called this a *"far-fetched indication"* because bone marrow is not commonly used (this seemed institution-dependent, in our view, as others in the group expressed that the field may be turning back somewhat to use of bone marrow). Peripheral blood transplant was viewed as a less realistic indication for ProHema, given the relatively short engraftment time associated with this source already. One of our experts pointed out that more generally, MAB conditioning is associated with longer engraftment times compared with RIC, and thus this may provide another potential segment focus, irrespective of cell source.

ProHema use in autologous transplants: With regard to autologous transplantation, all of our consultants were uniformly skeptical about the application of ProHema. They were aligned in citing a typical engraftment time of ~10 days for autologous transplantation and in doubting any substantial improvement on this; *"engraftment times are already so good, it's hard to make it better, how much more can you improve it?"*

Our consultants were aligned in thinking that meaningful adoption of ProHema outside of UCBT would require further benefit demonstrated in outcomes other than time to engraftment, which was nevertheless viewed as of primary interest. As one of our experts commented, *"there probably needs to be something more."* When probed on endpoints which could be differentiating, our consultants enumerated: **1)** time to neutrophil engraftment/hematopoietic recovery, **2)** time to platelet recovery and transfusion requirement, **3)** length of hospital stay, **4)** GVHD and infection rates, **5)** transplant-related mortality (TRM), **6)** relapse rate, and **7)** disease-free survival (DFS). Changes in these outcomes were considered by our experts to be impactful and as potentially driving adoption, though it was acknowledged that relapse and DFS are very disease-specific *("depends on the patient, not the process")*.

Summary of Consultants' Views on ProHema as a Potential Treatment Option in HSCT

Question	Consultant 1	Consultant 2	Consultant 3	Consultant 4	Consultant 5
Growth of UCB as HSC source in HSCT	Increasing	Increasing	Flat	Flat	Flat, but depends on center
Ease of ProHema incorporation into HSCT process	Easy	Easy	Easy	Easy	Easy
View on ProHema data to date	Improvement in time to engraftment clinically meaningful; noted preferential engraftment of ProHema unit as positive	Improvement in time to engraftment clinically meaningful	Would like to see more improvement in time to engraftment (7 days); noted preferential engraftment of ProHema unit as positive	Would like to see more improvement in time to engraftment (7-10 days)	Reasonable time to engraftment, but not viewed as very rapid
Chance of ProHema approval	Reasonable	Reasonable	Reasonable	Reasonable	Reasonable
Chance of ProHema uptake if approved	Good	Good	Reasonable (some physicians may feel uneasy about something new)	Reasonable (thinks faster time to hematopoietic recovery needs to be shown for uptake)	Good
Acceptable incremental cost of ProHema	Depends on overall cost-effectiveness ratio	Should be less than price for double cord blood transplant	Quoted additional $10,000 as theoretical threshold	$50,000-$75,000 is way out of range	$50,000-$75,000 is expensive, but could be reasonable, depending on outcome improvements
Potential applicability of ProHema platform to HSCT with peripheral blood	Probably not	Maybe	Probably not	Probably not	No
Potential applicability of ProHema platform to HSCT with bone marrow	Yes	Maybe	Yes	Probably not	No
Potential applicability of ProHema platform to autologous HSCT	No	Probably not	No	No	No
Comparison of ProHema to *ex-vivo* cord blood expansion strategies	Better (less laborious, less time-consuming, probably less expensive)	Better (less laborious, less time-consuming, probably less expensive)	Better (less laborious, less time-consuming, probably less expensive)	Better (less laborious, less time-consuming, probably less expensive)	Better (less laborious, less time-consuming, probably less expensive)
View of haploidentical transplant as competitor to UCBT	Yes	Not specifically discussed	Yes	Yes	Yes

Source: Cowen and Company, Consultant interviews

Hematopoietic Stem Cell Transplantation: Brief Overview

In February 2013, the Worldwide Network for Blood and Marrow Transplantation (WBMT) announced that the 1 millionth HSCT had been performed in late December 2012. Dr. E. Donnall Thomas performed the first successful bone marrow transplantation in 1956 at the Mary Imogene Bassett Hospital in Cooperstown, New York between identical twins for the treatment of leukemia. In 1957, Thomas published findings from a small case series of 6 patients with hematologic malignancies and bone metastases from cancer, whom he treated with bone marrow collected from fetal and adult cadavers, ribs removed at surgery, and aspiration biopsies (Thomas ED et al., *New England Journal of Medicine* 1957). As he wrote, *"The observations made in this small series of 6 patients confirm older clinical reports of the safety of intravenous infusion of suspensions of marrow cells."* In 1990, Thomas was awarded the Nobel Prize in Medicine.

According to the WBMT, which collects and analyzes global HSCT data from more than 70 countries and is a non-governmental organization recognized by the World Health Organization, in a 2013 statement, there are more than 50,000 patients undergoing HSCT annually, of which 53% are autologous transplants and 47% are allogeneic. In 2013, the WBMT published the results of a retrospective, global observational study evaluating HSCT

procedures performed in the 3-year period from 2006 to 2008 (Gratwohl A et al., *Haematologica* 2013). Data were collected from 1,411 teams in 72 countries. During the 3-year period, there were 146,808 patients who underwent a first HSCT, of which 45% were allogeneic transplants and 55% were autologous. Considered worldwide, HSCT procedures were most common in Europe (50%, of which 39% were allogeneic) and then in the Americas (29%, of which 46% were allogeneic).

Global HSCT Procedures During Three-Year Period From 2006-2008

	Americas		Europe		East Med/Africa		Asia/Western Pacific		Total	
	n	%	n	%	n	%	n	%	n	%
Allogeneic HSCT	**19,463**	**46**	**28,707**	**39**	**2,509**	**63**	**15,547**	**60**	**66,226**	**45**
Family donor	10,034	52	14,523	51	2,474	99	7,944	51	34,975	53
Unrelated donor	9,429	48	14,184	49	35	1	7,603	49	31,251	47
Autologous HSCT	**23,007**	**54**	**45,714**	**61**	**1,477**	**37**	**10,384**	**40**	**80,582**	**55**
Total	42,470	29	74,421	50	3,986	3	25,931	18	146,808	100

Source: Cowen and Company; Gratwohl A et al., *Haematologica* 2013

Overall, the main indications for HSCT were lymphoproliferative disorders (53%) and leukemias (36%), with solid tumors (5%) and non-malignant disorders (6%) being less common. When stratified according to type of HSCT, the main indications for allogeneic HSCT were leukemias (72%), lymphoproliferative disorders (15%), and non-malignant disorders (12%). For autologous HSCT, in contrast, lymphoproliferative disorders (84%) were the most common indication, followed by solid tumors (9%) and non-malignant disorders (1%).

Main Indications for Allogeneic HSCT

	Americas		Europe		Total	
	n	%	n	%	n	%
Leukemias	**13,620**	**70**	**20,476**	**71**	**47,677**	**72**
Acute leukemia	9,619	71	14,271	70	34,534	72
Chronic leukemia	1,827	13	2,259	11	5,448	11
MDS/MPS	2,174	16	3,946	19	7,695	16
Lymphoproliferative	**3,414**	**18**	**4,868**	**17**	**9,844**	**15**
Lymphoma	2,729	80	3,347	69	7,424	75
Plasma cell disorders	685	20	1,521	31	2,420	25
Non-malignant disorders	**2,192**	**11**	**2,954**	**10**	**7,821**	**12**
Bone marrow failure	1,247	57	1,359	46	4,168	53
Other non-malignant	945	43	1,595	54	3,653	47
Solid tumors	65	0.3	199	1	399	0.6
Other	172	1	210	1	485	1

Source: Cowen and Company; Gratwohl A et al., *Haematologica* 2013

Data on stem cell sources were available for 142,822 patients in the study. For autologous HSCT, peripheral blood was the predominant stem cell source, accounting for 98% of cases, while bone marrow use was minimal (2%). In allogeneic HSCT, peripheral blood was again the most common source (64%), followed by bone marrow (26%) and cord blood (10%). Allogeneic HSCT was performed with utilization of family donors in 51% of cases and unrelated donors in 49%, with cord blood accounting for 19% of sources in unrelated HSCT.

The annual number of HSCT procedures increased 10% from 46,563 in 2006 to 51,536 in 2008. There was a 26% increase in the median number of transplants per year performed at each clinical center, from 38 (2006) to 48 (2008). During this time, the relative increase for allogeneic HSCT of 17% was greater than the 5% increase in autologous HSCT. There were also changes noted in the use of stem cell sources, with the greatest relative increase (~30%) being in the use of cord blood.

HSCT Procedure Details

Broadly, HSCT is categorized as **autologous** *(patients receive their own stem cells)* or **allogeneic** *(patients receive stem cells from a related or unrelated donor)*. Transplanted hematopoietic stem cells (HSCs) replace stem cells which have been destroyed by systemic treatments. They also restore the hematopoietic system so that healthy blood cells can be produced.

Sources of HSCs: There are three sources of HSCs: **1)** bone marrow, **2)** peripheral blood, and **3)** umbilical cord blood. The procedure for collecting HSCs from bone marrow is known as **harvesting**, and is an approximately hour-long procedure conducted under general or regional anesthesia. Bone marrow is aspirated with a needle, most commonly from the pelvic bone. Once aspirated, the marrow is filtered to remove blood and bone fragments. The HSCs may then be cryopreserved *(combined with a preservative and frozen until needed)*. When peripheral blood is used as a source, an approximately 4-6 hour procedure known as **apheresis** is performed, in which blood is removed through a large vein and then processed through a machine which removes the HSCs, after which the blood is returned to the donor. Donors may be administered a growth factor drug (e.g., Neupogen) a few days prior to the procedure, in order to boost the number of stem cells in the blood. For umbilical cord blood as a source, upon the birth of a baby, blood is collected from the umbilical cord and placenta. It is then processed for HSCs.

The three HSC sources differ in terms of properties and potential effects on transplant outcomes. Previously, retrospective data from the Center for International Blood and Marrow Transplant Research (CIBMTR) have been reported, comparing graft (HSC) source and outcome effects for unrelated donor HSCT in 1,525 leukemia patients transplanted using cord blood, peripheral blood, and bone marrow (Eapen M et al., *Lancet Oncology* 2010). A topline comparison follows in the chart below.

Topline Comparison of HSC Sources

HSC Source, Unrelated Donor				
	Peripheral Blood	**Bone Marrow**	**Umbilical Cord Blood**	**Other Factors**
Rapid availability	Less rapid	Less rapid	More rapid	-
HLA match flexibility	Less flexible (7-8/8)	Less flexible (7-8/8)	More flexible (4-6/6)	-
Cell dose	Higher	Higher	Lower	-
Hematopoietic recovery (time to neutrophil engraftment)	Faster (median ~14 days)	Faster (median ~19 days)	Slower (median ~24 days)	-
Acute and chronic GVHD	Higher risk	Higher risk	Lower risk	-
Transplant-related mortality (TRM)	Lower risk (with perfect match), otherwise comparable (with mismatch)	Lower risk (with perfect match), otherwise comparable (with mismatch)	Higher risk (vs. 8/8 matched PB and BM), otherwise comparable (vs. 7/8 matched PB and BM)	Age at transplantation and disease (remission) status
Relapse	Comparable	Comparable	Comparable	Disease (remission) status
Disease-free survival	Comparable	Comparable	Comparable	Disease (remission) status

Source: Cowen and Company; Eapen M et al., *Lancet Oncology* 2010

Matching of Donors and Recipients: In order to minimize potential side effects in allogeneic HSCT, recipients of HSCs are matched as closely as possible with donors. **HLAs** *(Human Leukocyte Antigens)* are proteins expressed on the surface of an individual's cells which determine immunologic identity *(i.e., identify self vs. non-self)*. The major groups of HLAs are HLA-A, HLA-B, HLA-C, and HLA-DR, each of which has multiple proteins comprising it. In an individual, one set of HLAs is inherited from each parent *(there are 2 copies of each antigen group; for the four HLA groups, this would mean 8 antigens in an individual)*. Given this, among siblings, there is a 25% chance of having an identical set of HLAs, a 25% chance of not sharing any HLAs, and a 50% chance of having one of two HLA sets in common. Only 30% of patients requiring allogeneic HSCT have a matched sibling donor, which is the ideal scenario. According to the National Cancer Institute, the chance of receiving HLA-matched HSCs from an unrelated donor is ~50%. For unrelated individuals, the chance of HLA-matching is improved when race and ethnicity are the same. The chance of a transplant's success is correlated with the number of matching HLA antigens between a recipient and donor, with a perfect match *(i.e., "8/8")* being the best scenario. Allogeneic HSCT may be categorized by donor status as: matched related donor **(MRD)**, matched unrelated donor **(MUD)**, mismatched related donor **(MMRD)**, or mismatched unrelated donor **(MMUD)**.

Conditioning: Conditioning refers to the delivery of chemotherapy (and possibly radiation) to destroy cancer cells and suppress immunity by severely or completely depleting bone marrow cells ***(myeloablative)***, in preparation for receiving stem cells. Traditionally, extremely high doses of chemotherapy are used. Infused stem cells then restore blood cell production and immunity. **Reduced-intensity conditioning (RIC)** uses lower, less toxic doses of chemotherapy (and/or radiation) in a ***non-myeloablative*** regimen. With a non-myeloablative regimen, the bone marrow of the recipient, as well as cancer cells (in a malignancy indication), are not totally depleted, and the immune system is not totally suppressed. Cells from the donor and recipient co-exist for some time, until donor cells take over the bone marrow. For cancer treatment, the success of RIC is based on the ***graft-versus-malignancy*** (GVM) effect of allogeneic transplantation, in which donor cells recognize any remaining cancer cells and destroy them. RIC may allow SCT in otherwise ineligible patients, such as the elderly and

those with comorbidities. Because a recipient's own stem cells are not totally destroyed, blood cell counts are maintained in a higher range than would result following a myeloablative regimen. According to our consultants, the use of RIC regimens has become more common now, accounting for ~60% of conditioning used for transplants.

Transplant Procedure: For the HSCT procedure, the patient is typically admitted to the hospital. The duration of conditioning depends upon the type of regimen used, with MAB conditioning potentially lasting 3-4 weeks and RIC being shorter, about 1 week, according to our consultants. RIC may possibly be performed as an outpatient treatment. After the conditioning is completed, HSCs are infused within 24 to 48 hours. Processing of the cells (including thawing and washing, if frozen) is completed in the laboratory. The **infusion** procedure itself is not complicated, and is similar to receiving a blood transfusion, usually lasting a couple of hours. Side effects during infusion are rare and usually mild. These can include fever, chills, hives, coughing, low blood pressure, and fatigue. The **recovery** period begins after the infusion. The length of recovery post-transplant depends on the degree of conditioning utilized. Patients who have had intense or intermediate ablative conditioning remain in the hospital until the return of normal blood cell counts. This may take on average approximately 21 days. Post-RIC, it may be possible to be discharged home the day following the transplant, since the lower intensity of conditioning will not decrease blood counts as drastically. During the recovery period, patients are treated with prophylactic antibiotics and anti-viral medications, immunosuppressant drugs, and transfusions of blood products (red blood cells and platelets) as needed.

Complications: Potential shorter-term complications after HSCT include infection, bleeding, easy bruising, pneumonitis (lung inflammation), respiratory problems, and graft failure. Longer-term issues can be related to many factors, such as the conditioning regimen, other medications used during transplant, patient age, and pre-existing comorbidities. The complications can include organ damage (liver, kidneys, lungs, heart), infertility, disease relapse, and secondary malignancies. Once of the most concerning complications after transplant is GVHD.

Graft-Versus-Host Disease (GVHD): GVHD is a complication which may occur following allogeneic HSCT. It is a reaction of the donor immune system against recipient tissue. This complication develops when transplanted donor T-cells *(i.e., the graft)* recognize the recipient's *(i.e., the host)* normal cells (host antigens) as foreign and immunologically attack them. Traditionally, acute and chronic GVHD have been defined by time post-transplant, < 100 days or > 100 days, respectively. Current consensus, however, is that these conditions are better defined by clinical manifestations.

Acute GVHD typically involves the skin (~80% of patients), liver, or gastrointestinal tract (~50% of patients). It is staged and graded by the number and extent of organ involvement. **Chronic GVHD** can involve almost any organ, and is typically classified as **mild**, **moderate**, or **severe**, depending on severity of symptoms and number of organ systems affected. Common symptoms include skin rash, jaundice, nausea, vomiting, diarrhea, abdominal cramping, and increased dryness/irritation of the eyes. Risk factors for GVHD development include HLA-

mismatched related donor, HLA-matched unrelated donor, donor-recipient gender difference, pregnancy history in a female donor, and advanced donor or recipient age. Patients usually receive prophylactic treatment with immunosuppressants (e.g., calcineurin inhibitors and mTOR inhibitors). Typically, GVHD is treated with systemic steroids and additional immunosuppressive therapy as needed.

Acute GVHD Staging and Grading

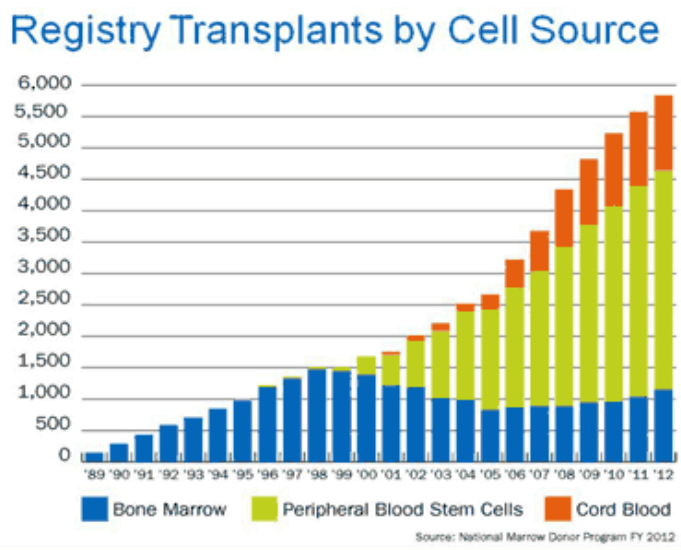
	Skin	Liver	GI
Stage			
1	Rash on < 25% of skin	Total bilirubin 2–3 mg/dL	Diarrhea > 500 mL/day or persistent nausea
2	Rash 25–50% of skin	Total bilirubin 3–6 mg/dL	Diarrhea > 1,000 mL/day
3	Rash > 50% of skin	Total bilirubin 6–15 mg/dL	Diarrhea > 1,500 mL/day
4	Generalized erythroderma with bullous formation	Total bilirubin >15 mg/dL	Severe abdominal pain with or without ileus
Grade			
I	Stage 1–2	None	None
II	Stage 3 or	Stage 1 or	Stage 1
III	-	Stage 2–3 or	Stage 2–4
IV	Stage 4 or	Stage 4	-

Source: Cowen and Company, Bolanos-Meade J et al., *Clinical Advances in Hematology & Oncology* 2004

Umbilical Cord Blood As a HSC Source

The first UCBT was performed in 1989 for treatment of Fanconi anemia in a child. Since then, more than 25,000 UCBTs have been performed worldwide, and more than 500,000 CBUs have been donated for public use. The use of UCB as a source of HSCs has been increasing over time, filling a need for an alternative cell source in HSCT. Though cooperative international donor registries have millions of volunteers, it has been estimated that, while most white patients (60%) will be able to find a MUD, a more limited number of African-American and minority patients (20%-45%) will do so. According to data from the National Marrow Donor Program (NMDP, which operates the US national donor registry under federal contract from the Department of Health and Human Services), during FY2012, there were cord blood units used in 1,191 registry transplants. In that same period, there were 3,400 registry transplants with peripheral blood stem cells and 1,150 registry transplants using bone marrow.

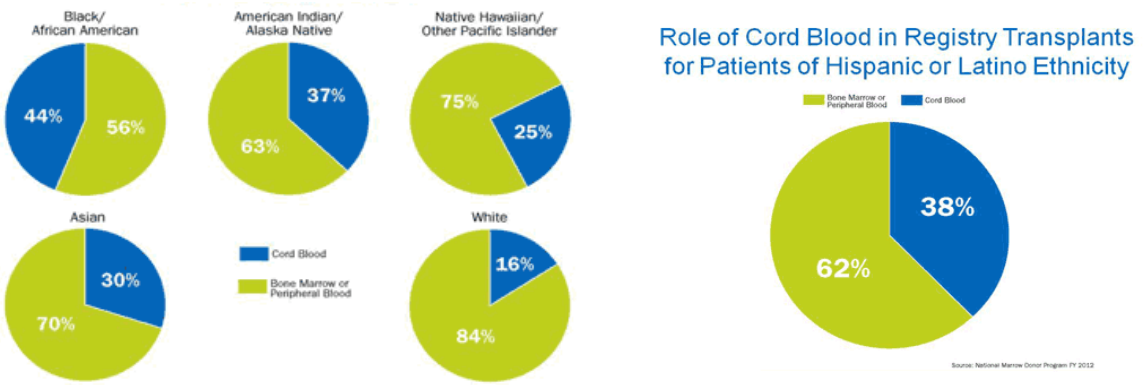
Cell Sources for NMDP Registry Transplants



Source: US Department of Health and Human Services; National Marrow Donor Program

Advantages of UCB as HSC Source: The advantages of UCB include: **1)** ease of HSC collection, with little to no risk to donor (mother or baby); **2)** prompt availability of cells; **3)** increased flexibility in HLA matching requirements; **4)** low risk of infection transmission; and **5)** relatively lower GVHD risk. The availability of cryopreserved UCB eliminates the risk of donor unavailability, allowing the transplant procedure to be scheduled according to the needs of the patient. On a HLA match level, there is decreased incidence of GVHD compared to other unrelated HSC sources, but with retention of graft-versus-malignancy effect. This increases the accessibility of transplantation to patients (especially minorities) who have no suitable unrelated donors. It is thought that the reduced incidence of GVHD with more HLA mismatches in UCBT results from the lower number of T-cells and the relatively naïve immune status of lymphocytes in UCB.

Cord Blood Use in Registry Transplants by Race/Ethnicity, FY 2012



Source: US Department of Health and Human Services; National Marrow Donor Program

Disadvantages of UCB as HSC Source: The disadvantages of UCB include: **1)** limited cell dose; **2)** longer time to engraftment of neutrophils and platelets compared to other sources (bone marrow or peripheral blood), with potential, therefore, for longer hospital stay; **3)** inability to obtain additional collections from donor; and **4)** disadvantaged immune reconstitution, given the relatively naïve immune system of the fetal source and the smaller number of mature immune cells. The major limitation of UCB is the relatively low **total nucleated cell (TNC) dose/kg** of recipient body weight provided. Lower cell dose has negative impacts on engraftment, transplant-related mortality, and survival. This especially becomes an issue with larger body weight (i.e., adult recipients and larger children). In an analysis of over 1,000 patients treated with single UCBT for hematologic malignancies (Barker JN et al., *Blood* 2010), evaluating impact of TNC dose and HLA match on outcomes, guidelines for selection of CBUs were suggested, prioritizing first completely matched units, followed by units with 1 mismatch and TNC > 2.5 x 10^7/kg, or units with 2 mismatches and TNC > 5.0 x 10^7/kg.

As most adults do not have access to a single CBU containing the recommended 2.5 x 10^7/kg cell dose, one method to overcome this potential limitation is the use of **double UCBT**, in which two CBUs are infused sequentially. This has enabled more adults to be treated with UCBT. Typically, only one of the infused CBUs dominates, the *"winning"* unit, and is ultimately responsible for long-term hematopoiesis after engraftment. The biological reasons for this one-unit dominance are not clearly understood, and the *"winner"* cannot be predetermined currently. The disadvantages of double UCBT include a potentially higher risk of acute GVHD as well as the increased cost *(CBUs are purchased from public cord blood banks)* relative to single UCBT.

Competitive Approaches in Development for CBU Enhancement

There are multiple approaches being investigated for enhancement of UCB as a HSC source to compensate for potentially limited cell numbers. Strategies for UCB enhancement include A) improvement in homing of HSCs, and B) *ex vivo* expansion of HSC numbers. Most of these approaches are in early stages of development. The strategies targeting improvement in homing, which more directly compete with the ProHema strategy, include 1) DPP-4 inhibition, 2) fucosylation with fucosyltransferase, and 3) complement C3a priming.

A) Enhancement of Homing

1) CD26/DPP-4 Inhibition: Dipeptidyl peptidase IV (DPP-4), also known as CD26, is an enzyme which is expressed on HSCs. DPP-4 cleaves the chemokine, stromal cell-derived factor-1 (SDF-1), which is a chemotactic, homing, and survival molecule for HSCs. Truncated SDF-1 cannot activate its receptor, CXCR4. Inhibition of DPP-4 enhances homing of HSCs toward endogenous bone marrow SDF-1. In preclinical animal studies (Broxmeyer HE et al., *Nature Medicine* 2012), mice were treated with the DPP-4 inhibitor sitagliptin or vehicle control before being irradiated. Recovery of bone marrow cellularity 7 days following radiation was significantly increased in mice treated with sitagliptin. Compared to vehicle-control mice, there was a 1.5-1.7x increase in long-term HSCs in the marrow of sitagliptin-treated mice. In a further mouse model of transplantation, recipient mice were pre-treated with sitagliptin and lethally irradiated. Marrow cells from donor mice were then administered. Engraftment was significantly greater ($p<0.05$) in sitagliptin-treated recipient mice.

Phase II Trial of Sitagliptin in UCBT: Investigators at Indiana University have conducted a Phase II pilot trial of DPP-4 inhibition with sitagliptin to enhance engraftment of single UCBT in adults with high risk hematologic malignancies. Sitagliptin (Januvia, Merck) is a DPP-4 inhibitor which is FDA approved as a treatment for type 2 diabetes. Results of the trial have recently been published (Farag SS et al., *Stem Cells and Development* 2013). There were 24 patients enrolled, age 21-58 years, with high risk leukemia or lymphoma, who received MAB conditioning. Single UCB units, with ≥ 4/6 HLA matches and minimum TNC dose of 2.5 x 10^7/kg, were used for transplantation. The primary endpoint of the trial was the proportion of patients engrafting by Day 30.

Efficacy Data: Patients received oral sitagliptin 600 mg once daily, one day before and for two days after transplant. Engraftment was defined as achievement of absolute neutrophil count (ANC) > 0.5 x 10^9/L for 3 consecutive days with donor derived cells. Platelet recovery was defined as achievement of platelet count > 20 x 10^9/L without transfusion for 7 consecutive days. There were 17 patients who received red cell-depleted (RCD) CBU grafts (the remaining 7 received red cell-replete, plasma-depleted grafts). The median time to neutrophil engraftment was 21 days (range, 13-50 days), and the cumulative incidences of engraftment by Day 30 and Day 50 were 88% and 94%, respectively. There was median 100% donor chimerism at the time of engraftment (range, 74%-100%). The median time to platelet recovery was 77 days

(range, 48-220 days). At a median follow-up of 259 days, the median event-free survival (EFS) and OS were both 606 days. The 1-year EFS rate was 53%, and the 1-year OS rate was 59%.

Safety Data: There were 4 deaths in the 17-patient RCD group resulting from infections and 1 death from relapse of leukemia. Only 1 patient in this group developed Grade II acute GVHD, which occurred while tapering immunosuppression. Grade 3/4 AEs in all patients included GI problems (vomiting, diarrhea, oral mucositis; n=12), acute renal insufficiency (n=2), sinusoidal obstruction (n=3), thrombotic microangiopathy (n=3), and acute cholecystitis (n=1).

2) Fucosylation with Fucosyltransferase: The MD Anderson Cancer Center group is investigating UCB enhancement with fucosylation. The initial step in homing is the interaction of HSCs with the vascular endothelium of the hematopoietic microenvironment in the bone marrow, which is at least partially mediated by P- and E-selectins *(adhesion molecules)* expressed on bone marrow endothelium and selectin ligands expressed by HSCs, including P-selectin glycoprotein ligand-1 (PSGL-1), also known as CD162. Carbohydrate modification (fucosylation) of selectin ligands is necessary for this interaction. Cord blood HSCs have decreased ability to bind selectins, as a large proportion express a nonfunctional form of PSGL-1 resulting from reduced expression and activity of fucosyltransferase, an enzyme which adds fucosyl groups to selectin ligands, making them fully functional.

Results from preclinical animal studies have been published (Robinson SN et al., *Experimental Hematology* 2012). In a mouse model of transplantation, human HSCs from cord blood were divided into two fractions, with half of the cells undergoing a 30-minute *ex-vivo* incubation with fucosyltransferase-VI (FT-VI) to increase fucosylation. This treatment increased the proportion of fucosylated cells to > 90%. Cells were then injected into groups of sublethally irradiated mice. At 7 days post-transplant, for mice transplanted with FT-VI-mediated, fucosylated cells, there were significant increases in human myeloid (4.4x, $p<0.001$), erythroid (8.1x, $p=0.008$), and multipotent (6.5x, $p<0.001$) stem cells in the bone marrow, compared to mice receiving untreated cells. Similar trends were observed at 14 days and 21 days post-transplant. At > 6 weeks, the levels of human engraftment in bone marrow and spleen of the mice were greater with animals receiving fucosylated cells (4% and 5%, respectively) compared to those receiving unfucosylated cells (0.05% and 0.25%, respectively).

Phase I Trial: A Phase I trial is currently ongoing at the MD Anderson Cancer Center, evaluating enhancement of CBUs with fucosylation in patients undergoing HSCT after both RIC and MAB conditioning. Eligible patients are age 1-80 years and have diagnoses of leukemia or lymphoma. Patients will undergo double UCBT, with one CBU which has been treated with fucosylation and one untreated CBU. The primary endpoints of the trial are the median time to neutrophil engraftment and the proportion of patients with engraftment within 42 days. The trial has an estimated enrollment of 50 patients, and is expected to be completed in July 2015.

3) Complement C3 Priming: The potential role of complement component C3 in HSC engraftment has been evaluated. Protein components of complement are activated through proteolysis. C3a and C3b are the first cleavage products of C3, and they bind to specific C3

receptors. The C3a receptor (C3aR) is expressed by HSCs, and activation of the receptor sensitizes the cells to SDF-1 (the SDF-1-CXCR4 axis), influencing the homing of the cells to bone marrow. In preclinical animal studies (Ratajczak MZ et al., *Leukemia* 2004), mice deficient in C3 were compared with wild-type mice. Upon transplantation of wild-type HSCs into C3-deficient mice, there were delays of 12 days in cell recovery in the spleen, 5-7 days in platelet and white blood cell recovery, and 16 days in cell recovery in the bone marrow. HSCs from C3-deficient mice transplanted into irradiated wild-type mice engrafted normally.

Phase I Trial: Investigators at the University of Minnesota conducted a Phase I trial evaluating UCB priming with C3a. Results were presented at the BMT Tandem Meetings in 2012 (Brunstein CG et al., *Biology of Blood and Marrow Transplantation* 2012). The study enrolled 10 patients, age 30-68 years, with diagnoses of leukemia or lymphoma. After RIC conditioning, patients underwent double UCBT. The smaller CBU was incubated for 30 minutes and infused without washing after the unmanipulated unit. There were 9 patients with neutrophil recovery at a median of 9 days (range, 6-26 days). On Day 21, hematopoiesis was observed to be primarily derived from the CBU treated with C3a in 6 of 9 (67%) patients.

Further evaluation with a randomized, Phase II trial in the MAB conditioning setting is being planned.

B) Ex vivo HSC Expansion

Another strategy to overcome cell-dose limitation in UCBT which is being investigated is *ex-vivo* expansion of cells prior to infusion. Increased numbers of cells should shorten engraftment time and reduce engraftment failure. It is established that co-culturing of stem cells with stimulatory cytokines and growth factors can expand cell numbers. Common approaches include cytokine combinations with Stem Cell Factor (SCF), Thrombopoietin (TPO) and Flt3 ligand (FL), collectively abbreviated STF. More recently, multiple novel strategies for expansion of CBU have been investigated. These include the use of: 1) mesenchymal stromal cells, an essential part of the hematopoietic microenvironment; 2) Notch ligand, given the Notch signaling pathway regulates expansion and differentiation of HSCs; 3) copper chelation, as cellular copper has a regulatory role in HSC proliferation and differentiation, with copper reduction promoting expansion, and 4) nicotinamide (NAM), a form of vitamin B3 (niacin) which inhibits the deacetylase SIRT1 and thereby delays differentiation of HSCs, favoring self-renewal.

***Ex-vivo* HSC Expansion Strategies**

Agent	Institution or Company	Mechanism	Clinical Studies	Clinical Results	Reference	Next Steps
Mesenchymal Stromal Cell (MSC)/ Mesenchymal Precursor Cell (MPC)	M.D. Anderson Cancer Center; Mesoblast	*Ex-vivo* expansion of CBU with STRO-3+ MSCs for 14 days	Phase I: n=31 adults with hematologic malignancies; dUCBT, 1 unit expanded; compared to 80 historical controls with unmanipulated dUCBT	TNCs expanded by median 12.2x, CD34+ cells by median 30x; median cell dose with expansion 8.34 x 10^7 TNC/kg Median time to neutrophil engraftment 15 days vs. 24 days control (p<0.001)	de Lima M et al., *NEJM* 2012	Phase III trial planned
Notch	Fred Hutchinson Cancer Research Center, University of Washington	*Ex-vivo* expansion of CBU with Notch ligand for 16 days	Phase I: n=10, age 3-43 years with high risk acute leukemias; dUCBT, 1 unit expanded	TNCs expanded by average 562x Median time to neutrophil engraftment 16 days; 9/10 pts engrafted btwn 7-17 days	Delaney C et al., *Nature Medicine* 2010	Phase II trial planned
StemEx	Gamida Cell and Teva	*Ex-vivo* expansion of CBU with copper chelator tetraethylenepentamine (TEPA) for 21 days	Phase I/II: n=10, age 7-53 years with hematologic malignancies; single UCBT with 1 of 2 fractions expanded Phase II/III: n=101 with hematologic malignancies, 25 centers; single UCBT with 1 of 2 fractions expanded	**Phase I/II:** TNCs expanded by average 219x; 9/10 pts engrafted; median time to neutrophil and platelet engraftment 30 and 48 days **Phase II/III:** Primary endpt 100-day mortality 15.8% vs. 24.5% control (p=0.035); median time to neutrophil engraftment 21 days vs. 28 days control (p<0.0001), to platelet engraftment 54 days vs.105 days control (p=0.008); GIII-IV aGVHD 19% vs. 17% control (p=0.11)	de Lima M et al., *Bone Marrow Transplantation* 2008 Phase II/III results reported by Gamida Cell, April 2013	July 2013: FDA advised Gamida Cell to conduct a randomized, controlled, Phase III trial
NiCord	Gamida Cell	*Ex-vivo* expansion of CBU with nicotinamide (NAM)	Phase I/II: n=11, age 21-61 years with high risk hematologic malignancies; dUCBT, 1 unit expanded	Median time to neutrophil engraftment 10.5 days; 10/11 pts engrafted (8 with NiCord unit); at median follow up of 8 months, PFS and OS rates 90%; no GIII-IV aGVHD	Results reported by Gamida Cell and presented at BMT Tandem Meetings, February 2013	September 2013: Second Phase I/II trial initiated, evaluating single expanded UCBT, expected to enroll 20 adults with hematologic malignancies

Source: Cowen and Company

Alternative HSC Source: Haploidentical HSCT

One development in alternatively sourced HSCT has been the use of **haploidentical** related donors. A haploidentical transplant uses cells from a related donor which are partially HLA-mismatched and therefore not considered suitable under conventional standards. Haploidentical donors are sometimes called *"half-matched,"* as they have one haplotype *(a group of genes inherited together from a single parent)* matching the recipient *(thus, at least a half HLA-match)*. Parents and children are haploidentical *(always, since half of the genetic material comes from each parent)*, and there is a 50% chance that siblings will be haploidentical. Potential advantages of haploidentical HSCT include increased accessibility (*90% of patients will have a haploidentical family member)*, immediate donor availability, lack of ethnicity barrier, and ability to obtain additional cells if necessary.

One approach to haploidentical HSCT has been developed at Johns Hopkins in the non MAB setting, with the use of unmanipulated cells and high-dose cyclophosphamide after transplantation for T-cell depletion. Cyclophosphamide is administered at days 3 and 4 post-transplant in order to decrease alloreactive T-cells. Results with this approach in patients with hematologic malignancies have previously been described and published (Luznik L et al., *Biology of Blood and Marrow Transplantation* 2008; Fuchs E et al., *Current Opinion in Oncology* 2013). The median times to neutrophil and platelet recovery were noted as 15 days and 24 days, respectively, with a 34% incidence of Grade II-IV acute GVHD. Relapse rates have been in the 40%-50% range.

The Blood and Marrow Transplant Clinical Trials Network has conducted two prospective, parallel, multicenter, Phase II trials comparing transplant after RIC conditioning with double UCB (n=50) and haploidentical related bone marrow (n=50) in patients with leukemia or lymphoma and no related donors (Brunstein CG et al., *Blood* 2011). Haploidentical patients received post-transplant cyclophosphamide as described above. After dUCBT, the median time to neutrophil engraftment was 15 days (range, 4-47 days), and the median time to platelet recovery was 38 days (range 3-87 days). With haploidentical transplantation, the median time to neutrophil engraftment was 16 days (range 12-83 days), and the median time to platelet recovery was 24 days (range, 1-92 days). Overall, the 1-year OS and PFS probabilities were similar with both types of transplants: 54% and 46%, respectively, with dUCB compared to 62% and 48%, respectively, with haploidentical transplant. The 100-day cumulative incidence of Grade II-IV acute GVHD was 40% after dUCBT and 32% with haploidentical transplant. The 1-year non-relapse mortality and relapse rates with dUCBT were 24% and 31%, respectively. After haploidentical transplant, these rates were 7% and 45%, respectively. Based on these results, a multicenter, randomized, Phase III trial comparing dUCBT and haploidentical bone marrow transplant in patients with hematologic malignancies after RIC is now underway.

Comparison of Alternative HSC Sources

	MUD (Matched unrelated donor)	Haploidentical (mismatched related)	UCB (cord blood)
Availability	20–80%, depending upon recipient ethnicity	Nearly 100%	Nearly 100%
Cell dose	Collection targeted to recipient weight	Collection targeted to recipient weight	Fixed to amount in CBU
HLA match	7–8/8 (HLA- A, B, C, DRB1)	4–6/8 (HLA- A, B, C, DRB1)	4–6/6 (HLA- A, B, DRB1)
Time to find suitable donor	8–10 weeks	< 4 weeks	< 4 weeks
Time to neutrophil engraftment	15–20 days	15–20 days	20-30 days
Risk of graft failure	5%	5–10%	5–15%
Acute GVHD	50–80%	25–50%	25–60%
Chronic GVHD	50–60%	10–50%	30%
Additional cell therapy	Donor lymphocytes available if needed for delayed engraftment or relapse	Donor lymphocytes available to treat relapse; experience is limited	Not available

Source: Cowen and Company, Adapted from Fuchs E et al., *Current Opinion in Oncology* 2013

The Consultant's Corner: *What Do Our Consultants Think of Haploidentical HSCT?*

All of our consultants acknowledged that haploidentical HSCT is of increasing interest in the transplantation community, calling it the *"competitor"* and *"competing field"* to CBT. Given the data to date, they viewed haploidentical transplantation as a procedure with potentially increasing adoption because of its advantages in expanding donor possibilities and relative convenience, which overlap with the advantages of cord blood as a source.

One particular advantage of the haploidentical approach cited was lack of significant incremental cost *("the Cytoxan used after infusion costs less than $1,000")* to the overall procedure. In terms of disadvantages with haploidentical transplant, our consultants voiced concerns about disease relapse rates and infection. As one of our consultants summarized in comparing the two alternative HSC sources, *"cord blood has more problems at the front end, and haploidentical has more problems at the tail end."* He indicated that haploidentical transplant is easier than double UCBT upfront, stating that *"it is cheaper, easier, with faster recovery and shorter length of stay…it is a superior procedure in the first 3 months."*

However, in the longer-term, the two approaches to allogeneic transplant were viewed as becoming more equivalent. Thus, our expert felt that for cord blood to be considered a better approach than haploidentical transplant, improvements in outcomes would ideally be targeted for the shorter-term, in that upfront period; *"making cord blood better and cheaper in the first 3 months would create a procedure better than haploidentical."*

ProHema for Rare Genetic Disorders

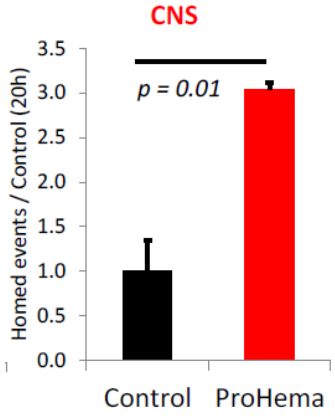
Fate is pursuing the potential use of pharmacologically modulated HSCs for allogeneic HSCT treatment of rare genetic disorders. The company is planning to evaluate ProHema in an initial clinical trial of pediatric patients with demyelinating lysosomal storage disorders (LSDs). Also, an active research program is being undertaken to develop a second generation HSC therapeutic which will be specifically designed to *enhance the homing of HSCs to the central nervous system (CNS)*, in order to enhance delivery of essential enzymes to patients with deficiencies.

ProHema Preclinical Study

A preclinical mouse model was used to evaluate homing and migration across the blood-brain barrier (BBB) into the CNS by HSCs. Mice were irradiated and then injected with either HSCs from human umbilical cord blood modulated with FT1050 (ProHema) or vehicle control for 2 hours. At 20 hours following the injections, DNA was isolated from the brain tissue of the mice, and the number of human cells in each sample was determined in order to evaluate CNS homing.

Results demonstrated that the number of homing events to the CNS was significantly increased with HSCs that were modulated with FT1050 (ProHema) compared to those treated with vehicle control. The number of homing events was approximately tripled with ProHema vs. control (p=0.01).

Preclinical Results: CNS Homing Events



Source: Fate Therapeutics Presentation, Fate S-1

What's Next for ProHema in LSDs? Fate has indicated that it plans to initiate the first clinical trial of ProHema in pediatric patients with demyelinating LSDs in 2H14, with a target to generate data in 2015. The trial will be initiated after filing of an IND amendment. The company has indicated that the current ProHema IND may cover this trial with an amendment, but has acknowledged that the FDA may require filing of a new IND.

Preliminary Plan for ProHema Clinical Trial in LSDs: Fate has discussed the potential design for this initial clinical trial. The trial will enroll patients from age 1 to 21 years. Post conditioning, patients will be treated with a ProHema CBU combined with an unmodulated unit. The initial cohort of patients will receive a standard MAB regimen of high-dose chemotherapy, with one agent having a 25% dose reduction. Subsequently, cohorts will receive conditioning regimens which are successively dose-reduced.

The primary endpoint of the trial will be neutrophil engraftment under a RIC regimen. Secondary endpoints will include other engraftment measures and safety. Enrolled patients will have regular cognitive and functional evaluations to evaluate developmental milestones after the HSCT procedure. The company anticipates that the trial will be conducted in 1 to 3 clinical centers specializing in pediatric cord blood transplantation for rare genetic disorders.

The Consultant's Corner: *What Do Our Consultants Think of ProHema for LSDs?*

Our consultants, three specialists in pediatric HSCT who treat patients with LSDs at a leading academic transplant center with a high volume of pediatric patients with rare, metabolic storage disorders, estimated the incidence of LSDs to be between 1 in 50,000 to 1 in 100,000 births. They emphasized that a wide range of diseases fall under the heading of LSDs, with each being "*biologically distinct*" and *"vastly different."* According to our experts, allogeneic HSCT is a mainstay of treatment *for some LSDs* and is able to halt or reduce disease progression. However, *in other LSDs*, HSCT is "*not effective*" and "*does not provide enough enzymatic activity*."

Our experts noted that the reasons for this disparate efficacy are unknown and vary by disease. Enzyme replacement therapy (ERT) is also available for some LSDs, and as noted by our consultants, should be instituted for any disease for which it is available; ***however, ERT is limited by the fact that it does not cross the blood-brain barrier (BBB) effectively***. As remarked by one of our experts, *"ERT can help with some symptomatology, but all LSDs have a neuronal component and all patients die of cerebral degeneration."* In our consultants' practices, ERT is part of a multimodal approach with HSCT.

Our experts estimated that ~60-80 allogeneic HSCT procedures for LSDs are performed annually in the US, with fewer, ~30-50, in Europe (at their institution, which is a leading transplant center with a high volume of LSD patients, there are approximately 12 transplants per year). They identified the common LSD indications as Hurler's syndrome (mucopolysaccharidosis I, MPS I), MPS III, Niemann-Pick disease, and Krabbe's disease (noted to be institution-dependent), with Hurler's being the most common. According to our experts, at least 50% or more of allogeneic HSCTs for LSDs utilize UCB, given that *"usually timing is an issue; you don't want to wait long because of neuronal progression."* They characterized the HSCT procedure for LSDs to be similar overall to HSCTs for other indications such as malignancy, other than the use of more disease-specific conditioning protocols (i.e., RIC). One noted difference regarded HSCT outcomes, which, in addition to standard transplant measures of engraftment and survival, include neurologic development

and cognitive measures from neuropsychiatric testing (described by one of our physicians as *"walking, talking, feeding themselves, having an elevated trajectory of learning, and getting back to school"*). The success of HSCT for LSDs was estimated to be 90%-100% with a sibling donor, and 70% with an unmatched (including UCB) donor. Allogeneic HSCT for LSDs, and in tandem the use of UCB, were viewed as increasing over time by our experts because of increased newborn screening, which *"picks up more patients earlier."*

Our consultants were familiar with ProHema and had generally positive views on the theoretical potential for pharmacologic modulation in the setting of HSCT for LSDs. One of our experts called ProHema *"a very good idea"* and felt that it may be relevant in LSD treatment, as *"it does work in the setting of regular homing to bone marrow…and the niche in CNS resembles the niche in bone marrow."* By this, he meant that the major drivers for homing and engraftment, including environmental permissiveness and molecular pathways, are similar in both tissues. As he stated, *"the same mechanisms apply at multiple sites in the body."*

Our second expert agreed on the rationale of ProHema in this setting and felt that it was a *"step in the right direction, as one of the goals of transplant is homing into the brain"* for LSDs. At the same time, while this expert noted the early ProHema data to be promising, he was also clear that *"the acceleration of engraftment was not a home run,"* referring to the Phase I trial result. He desired to see an improvement of 7 to 10 days.

Our third expert agreed that the improvement in hematopoietic recovery thus far of around 3 days may not in and of itself be game-changing, but he was more excited about seeing a potential increase in CNS homing, which "*may open transplant up to diseases which we are not currently transplanting"* and *"could be a big deal."*

With regard to the potential development program for ProHema in the LSD setting, our consultants agreed that they would first like to see further data in a clinically relevant disease model, with evidence not only of engraftment but also of function; *"can you show in a test that neurological and behavioral aspects are changed?"* This should also translate clinically, according to our physicians, into improved neurologic outcomes in patients. Our consultants were generally positive on the chance of success for ProHema development and ultimately approval. One expert believed that *"the likelihood of getting to the clinic is high,"* given the clinical program for malignancy already is running, with clinical data available. Our other expert did not foresee any regulatory problems and commented that there are *"no obvious red flags"* to date for ProHema. Our third consultant felt that it is "*certainly worth thinking about a trial."*

Our consultants were also positive about the potential for adoption of ProHema in LSD treatment, if approved. One described himself as *"optimistic about this program."* Our other experts remarked that the community is open to new strategies for better outcomes, as *"we are trying to push the field irregardless, and if something improves outcomes for our patients, we will use it."* When probed on the acceptable level of potential cost for ProHema, if approved, our consultants linked this to clinical evidence of improved neurologic function. *"Does it translate into better functioning? It depends on how significant the change would be,"* stated one of our physicians. Another expert also emphasized the importance of measured

neuropsychiatric outcomes. He opined that even a high cost (six-figure range, theoretically) would be acceptable *"if you find out how many I.Q. points you are adding…that's the bottom line…and you could put a price on it."*

Summary of Consultants' Views on ProHema as a Potential Treatment Option in HSCT for LSDs

Question	Consultant 1	Consultant 2	Consultant 3
Growth of allogeneic HSCT for LSDs	Increasing because of improved newborn screening	Increasing because of improved newborn screening	Increasing because of improved newborn screening
Growth of UCB as HSC source in HSCT for LSDs	Increasing	Increasing	Increasing
View on potential of ProHema in LSDs	Has potential	Has potential	Has potential
View on ProHema preclinical homing data	Intriguing, positive	Intriguing, positive	Intriguing, positive; excited about potential for improved homing to support HSCT for more LSDs
View on ProHema clinical data to date (Phase I data in malignancies)	Results so far promising; advantageous overall to have clinical results in another indication	Promising, but would like to see more improvement in time to engraftment (7-10 days)	Would like to see more improvement in time to engraftment
Chance of ProHema uptake if clinical development successful	Good	Good	Good
Acceptable incremental cost of ProHema in LSDs	Depends ultimately on improvement in neurocognitive functional outcomes	Depends ultimately on improvement in neurocognitive functional outcomes	Needs to be based on more compelling benefits than just time to engraftment

Source: Cowen and Company, Consultant interviews

Rare Genetic Disorders and HSCT: Brief Overview

Among other conditions, inborn errors of metabolism (IEM) include a significant subgroup categorized as lysosomal storage disorders (LSDs), rare genetic disorders resulting from mutations which lead to enzyme deficiencies that disturb lysosomal function *(lysosomes are subcellular organelles which break down and turnover cell contents)*, causing progressive multi-organ failure and early death through accumulation of toxic metabolites. With an incidence of approximately 1 in 50,000 to 1 in 100,000 births, depending on the disorder, LSDs encompass over 50 diseases, which vary in their spectrum of symptoms and age of onset. The majority are inherited in an autosomal recessive manner. The classic clinical presentation of a LSD is a neurodegenerative disease of infancy or childhood. The constellation of symptoms can include dysmorphic features (coarse facies, macroglossia), bone abnormalities, cardiac

abnormalities, liver and spleen enlargement, ophthalmologic signs (corneal clouding), and neurologic problems. LSDs can be broadly divided into the mucopolysaccharidoses, in which glycosaminoglycans are accumulated, and leukodystrophies (sphingolipidoses), caused by deficiencies in lysosomal acid hydrolases involved in sphingolipid metabolism.

A major development in treatment of LSDs has been the availability of enzyme replacement therapy (ERT) for some of the diseases. ERT replaces the deficient enzyme in the lysosome by delivering a functional, wild-type enzyme to the cell in the form of a recombinant protein. ERT is available for Gaucher disease, Fabry disease, mucopolysaccharidosis I (MPS I), MPS II, MPS VI, and Pompe disease. However, responses to ERT are variable, and therapy does not improve all aspects of the disease to the same degree. One significant limitation of ERT results from the inability of the replacement enzymes to cross the blood-brain barrier (BBB). Because of this, CNS disease cannot be adequately treated.

For more than 30 years, allogeneic HSCT has been used as a therapy for LSDs. The primary benefit of allogeneic HSCT is the replacement of missing enzyme produced from donor cells circulating in blood, as well as engraftment of donor HSCs *(microglia)* in the brain, which function as local sites of enzyme production. While HSCT has a relatively long history of use for these rare genetic disorders, sizeable clinical series only exist for a few conditions, including Hurler's syndrome and infantile Krabbe's disease. Historically, allogeneic HSCT for LSDs has been performed with bone marrow from matched or mismatched related donors. However, one limitation is the lack of a matched bone marrow donor for many children with these diseases. Thus, an alternative source used for HSCT in children with metabolic disorders is banked umbilical cord blood from unrelated donors.

Hurler's syndrome (HS) is the most severe form of the LSD mucopolysaccharidosis type I (MPS I), an autosomal recessive metabolic disorder resulting from deficiency of α-L-iduronidase, which results in the accumulation of heparan and dermatan sulfate substrates (glycosaminoglycans) in tissues. In severe cases, symptoms appear before the age of 2 years and lead to progressive, multisystem deterioration of the CNS, cardiac disease, skeletal abnormalities, corneal clouding, liver enlargement, and death in childhood. While ERT has been available for patients with MPS I since 2003, this does not prevent CNS deterioration. Allogeneic HSCT is considered the treatment of choice, and HS is the most common LSD for which transplant is performed, with more than 500 procedures worldwide to date.

Krabbe's disease, also known as globoid-cell leukodystrophy, is an autosomal recessive genetic disorder resulting from deficiency of the lysosomal enzyme galactocerebrosidase. This enzyme deficiency leads to decreased breakdown of galactolipids in myelin, which results in failure of myelination of the central and peripheral nervous systems, leading to rapid, progressive neurologic deterioration and death. Symptoms typically present before age six months and include irritability, spasticity, blindness, deafness, and seizures. Death typically occurs before age 2 years.

Allogeneic HSCT with Cord Blood for LSDs, COBLT Study: The Cord Blood Transplantation Study (COBLT) was sponsored by the National Heart, Lung, and Blood

Institute (NIH) and prospectively evaluated UCBT as a treatment for patients with hematologic malignancies and also for 69 children with LSDs. Results for LSD patients have been published (Martin PL et al., *Biology of Blood and Marrow Transplantation* 2006). The median age of patients in the study was 1.8 years. Among the primary diseases, the most highly represented were Hurler's syndrome (n=21) and Krabbe's disease (n=16). Almost all the patients (67/69) were treated at Duke University. After conditioning, patients were treated with a CBU providing the highest number of cells (1 x 10^7 TNC/kg) and with a minimum 4/6 HLA match. The primary endpoint of the trial was survival at 180 days post-transplant. Secondary endpoints included neutrophil and platelet engraftment, incidence of GVHD, and treatment-related mortality. Neutrophil engraftment was defined as ANC of at least 500/mcL for 3 consecutive measurements on different days and demonstrated donor chimerism of > 90%. Platelet engraftment was defined as platelet count of > 20,000/mcL for 3 consecutive days, unsupported by platelet transfusion for a minimum of 7 days.

COBLT Study Results: There was 80% survival overall at 180 days post-transplant, and 72% at one year. At a median follow-up of 24.5 months, the survival rate was 68%. The median time to neutrophil engraftment was 25 days. The cumulative incidence of engraftment by Day 42 was 78%. The median time to platelet engraftment was 88 days. There were 25 patients (36%) who developed Grade II to IV acute GVHD. The cumulative incidence of chronic GVHD at one year post-transplant was 18%. By Day 42 post-transplant, Grade 3/4 AEs included severe pulmonary toxicity (12%), severe CNS toxicity (10%), and severe stomatitis (6%). There was one fatal pulmonary toxicity.

The COBLT study did not assess effects on neurocognitive, language, and motor development. However, results after UCBT in 20 patients with HS (14 of whom were included in COBLT) have previously been reported (Staba SL et al., *New England Journal of Medicine* 2004). In this study, neutrophil and platelet engraftment occurred at a median of 24 days and 56 days, respectively. At a median follow-up of 905 days, there were 17/20 patients alive, all of whom had complete donor chimerism and normal peripheral blood α-L-iduronidase activity. It was reported that within 1-year post-transplant, the majority of patients had normal growth velocity. There were no children with clinically significant cardiac dysfunction, and all had either stable or improved neurocognitive function after transplantation, with the cognitive development slope increasing from 0.56 at age 24 months to 0.81 at 54 months and 0.95 at 72 months, compared to a slope of 1.0 in normal children.

Results after UCBT in 25 patients (11 asymptomatic and 14 symptomatic) with infantile Krabbe's disease (4 of whom were included in COBLT) have also been reported previously (Escolar ML et al., *New England Journal of Medicine* 2005). In this study, at a median follow-up of 3 years, there was 100% engraftment and 100% survival in asymptomatic newborns, and 100% engraftment but 43% survival in symptomatic infants. After transplantation in symptomatic patients, none had any appreciable neurodevelopmental improvement. However, in the asymptomatic group, 10 infants were evaluated after transplant, and all gained cognitive skills at a normal rate, with 9/10 having normal receptive language. In terms of gross motor function assessed at 4 to 66 months of age, four children had mild to severe delays in

development of motor skills, while six gained motor skills during the first year, two of whom continued normal development until age 2 and 3 years, respectively.

Duke University Study: Results from a large, single-center, Duke University study of 159 consecutive patients with LSDs undergoing UCBT from 1995 to 2007 have been published (Prasad VK et al., *Blood* 2008). The median age of patients was 1.5 years. Of the primary diagnoses, HS (n=45, 28%) and Krabbe disease (n=36, 23%) accounted for the largest patient proportions. After MAB conditioning, patients received UCBT, with the majority (152/159) having one to three HLA mismatches. The median follow-up was 4.2 years (range, 1-11 years). Neutrophil engraftment was defined as ANC of ≥ 500/mcL for 3 consecutive days, and platelet engraftment was defined as platelet count of 50,000/mcL for 7 days without transfusion.

Duke Study Results: The median time to neutrophil engraftment was 22 days (range, 10-76 days). The cumulative incidence of neutrophil engraftment by Day 42 was 87.1%. The median time to platelet engraftment was 87 days (range, 25-379 days). The cumulative incidence of platelet engraftment by Day 180 was 71%. A total of 95% of patients achieved > 90% donor chimerism. Serum enzyme levels normalized in 97% of evaluable patients. The estimated overall survival rates at 1, 3, and 5 years were 72%, 63%, and 58%, respectively. The 5-year survival rate in HS was 74.5%, and was 57% for Krabbe's disease. In 155 evaluable patients, Grade II, III, and IV acute GVHD occurred in 31%, 5%, and 5% of patients, respectively. Extensive chronic GVHD occurred in 11% of patients at 1 year, and 14% of patients at 2 years. In this publication, it was noted that the 45 HS patients had been followed for a median of 5.6 years. The authors reported that all surviving patients experienced disease stabilization, with most gaining cognitive skills. All children attended school, and 81% were in age-appropriate classes. However, orthopedic issues were noted to have progressed in many patients, with 11 patients undergoing surgical procedures for correction.

Fate's Wnt7a Program

Wnts (*Wingless* and *I*nt-1) comprise a family of 19 glycoproteins which mediate development primarily through binding with Frizzled (Fzd) transmembrane receptors. Wnts regulate differentiation during muscle fiber development, as well as in muscle regeneration. Wnts activate at least three different signaling pathways. In the canonical β-catenin pathway, Wnt binding to Fzd activates a cytoplasmic serine/threonine kinase and ultimately leads to stabilization of β-catenin. This pathway is involved in myogenic cell differentiation and development. In a non-canonical pathway, Wnt binding to Fzd stimulates calcium influx and activation of NFAT and PKC. An additional non-canonical pathway, known as planar cell polarity (PCP) is involved in establishing polarity of cells within a tissue *(polarity refers to the asymmetric organization of different aspects of the cell, including the surface, organelles, and cytoskeleton; cell polarity is responsible for diversification of cell function/type and regulation of stem cell division and differentiation)*. Signaling through the PCP pathway drives cell division of satellite stem cells in skeletal muscle through enhancement of stem cell polarization.

Skeletal muscle is composed of contractile muscle cells (myofibers) which form from precursor cells called myoblasts. **Satellite cells** are muscle stem cells. During development, the number of myofibers remains constant, while each myofiber grows in size by fusion of satellite cells. Adult skeletal muscle is typically stable, with occasional fusion of satellite cells, involved in muscle turnover from daily muscle use. However, skeletal muscle possesses regenerative capacity after injury. This process involves satellite cells and interaction with their environment, known as the stem cell niche.

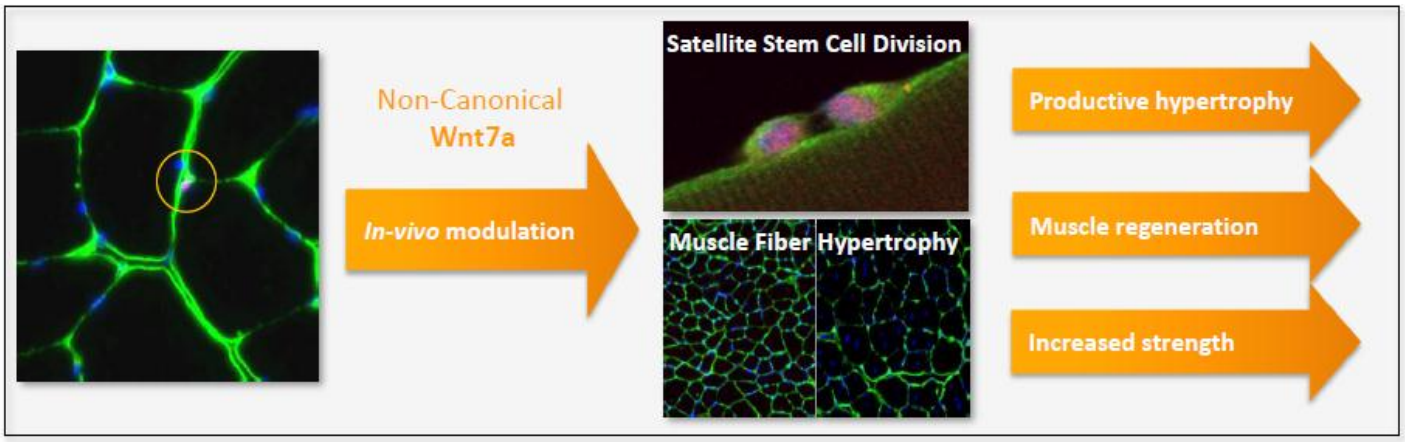
Like other adult stem cells, satellite cells are able to both replicate *(self-renew)* and differentiate, producing functional cells *(becoming myofibers in this case*). Satellite cells are heterogeneous and can differ in gene expression, differentiation potential, proliferative potential, and *"stemness" (i.e., behavior as true stem cells which can reconstitute the stem cell niche)*. Within this heterogeneity, there is a small population of true stem cells (**satellite stem cells, SSCs**) which are different from the population of satellite cells with more commitment to myogenic differentiation *(i.e., becoming functional muscle cells)*. SSCs are less committed to myogenic development and replicate to replenish the stem cell pool, ultimately producing more myogenic precursor cells which can function in skeletal muscle growth and regeneration.

Wnt signaling has an important role in the regulation of satellite cell replication. In particular, Wnt7a binding to its receptor Fzd7 activates the PCP pathway and stimulates the expansion of SSCs. This has a direct effect on the regenerative capacity of muscle. In *in vitro* studies with cell cultures of satellite-cell derived myoblasts, treatment with recombinant Wnt7a produced significant myofiber hypertrophy, with an associated increase in number of muscle cell nuclei (von Maltzahn J et al,. *Nature Cell Biology* 2012). Treatment with other Wnts (Wnt5a or Wnt3a) did not lead to similar hypertrophy. Wnt7a-Fzd7 signaling was observed to activate the PI3K/Akt/mTOR pathway, which is known to be involved in the regulation of skeletal muscle hypertrophy. Wnt7a treatment was noted to produce elevated levels of phosphorylated Akt and downstream protein target S6 in cell culture. Additionally, increased phosphorylation of PI3K, which is the direct activator of the downstream Akt/mTOR pathway, was observed. Application

of a mTOR inhibitor (rapamycin) blocked the development of muscle hypertrophy resulting from Wnt7a treatment. These preclinical results support the involvement of Wnt signaling, particularly through Wnt7a-Fzd7, in the regulation of molecular pathways of skeletal muscle growth.

Fate is developing a method of *in vivo* modulation of muscle satellite stem cells with a recombinant analog of Wnt7a for application in neuromuscular disease, such as muscular dystrophy. It is hypothesized that *in vivo* modulation may drive the expansion of satellite stem cells, thereby enhancing the regenerative capacity of muscle and potentially providing clinical benefit.

***In vivo* SSC Modulation**



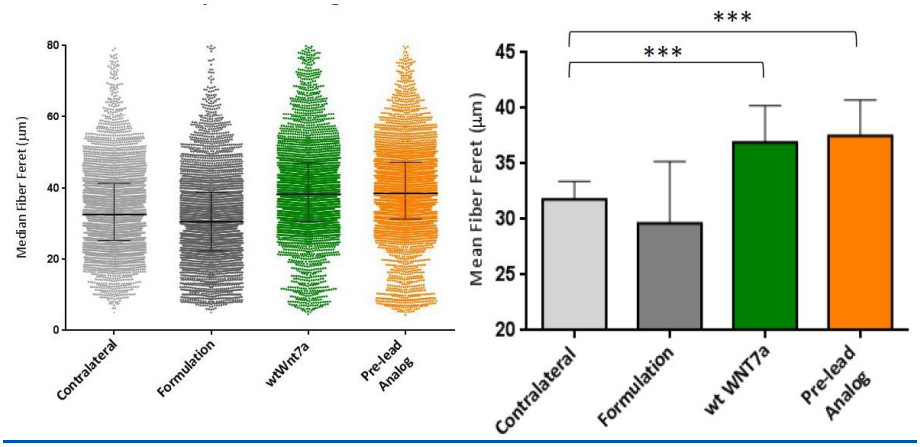
Source: Fate Therapeutics Presentation

Preclinical Studies with Wnt7a and Wnt7a analogs

In preclinical *in vivo* studies using a mouse model of muscular dystrophy *(mdx)* and wild-type mice, animals were administered a single injection of Wnt7a or a Wnt7a analog in the tibialis anterior muscle. Effects were compared to both a control formulation injection as well as to the untreated, opposite muscle in the mouse (the *"contralateral"* control).

Muscle Hypertrophy: At three weeks following injection, there was a significant muscle hypertrophy effect, as measured by average muscle fiber size, with the injection of Wnt7a or Wnt7a analog compared to the contralateral control ($p<0.01$) in 5/6 wild-type mice. There was about a 20% increase in median muscle fiber cross-sectional diameter *("Feret's diameter" is a measure of muscle fiber cross-sectional size)*.

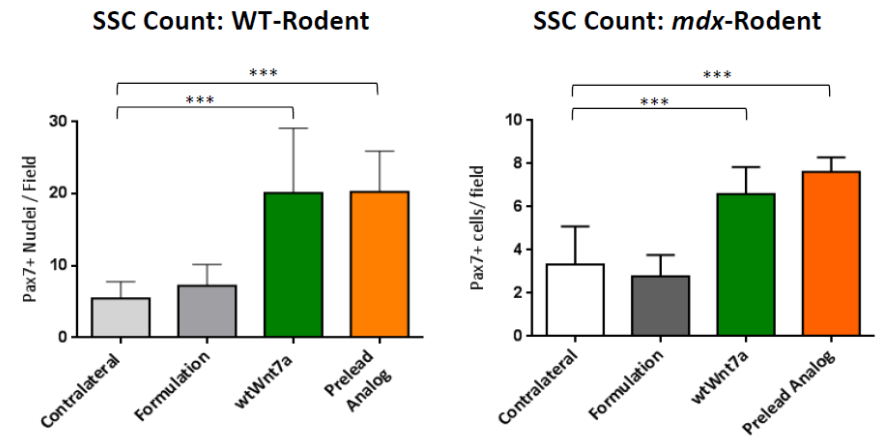
Preclinical Mouse Model: Muscle Hypertrophy Effect



Source: Fate Therapeutics Presentation, Fate S-1; ***p<0.01

SSC Expansion: The effects on *in vivo* expansion of the satellite stem cell (SSC) population were also evaluated, as identified by the number of Pax7-positive cell nuclei, a marker for SSCs. In both wild-type and *mdx* mice (5/6 in both groups), at 3 weeks after injection, there was a significant, ~3-fold increase in SSCs (Pax7+ nuclei) in muscle treated with Wnt7a or analog when compared to the contralateral control (p<0.01).

Preclinical Mouse Model: SSC Expansion

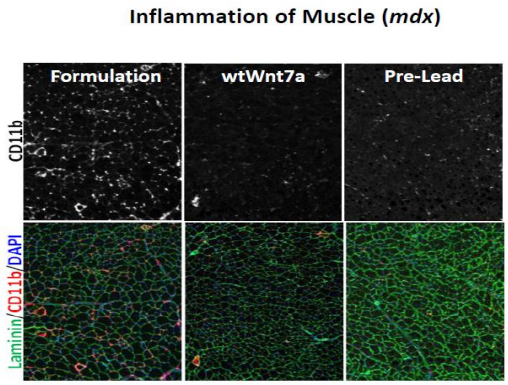


Source: Fate Therapeutics Presentation, Fate S-1; ***p<0.01

Muscle Damage and Inflammation: In further preclinical studies with the *mdx* mouse model, potential effects of Wnt7a administration on muscle damage and inflammation were evaluated. Muscle fiber necrosis was measured as the mean IgG+ fibers per unit area of muscle. Inflammatory infiltration was measured by staining of CD11b, a marker of cellular inflammation, within mouse muscle. After a single injection of Wnt7a or Wnt7a analog, compared to formulation control, there was a significant reduction in muscle fiber necrosis observed in 5/7

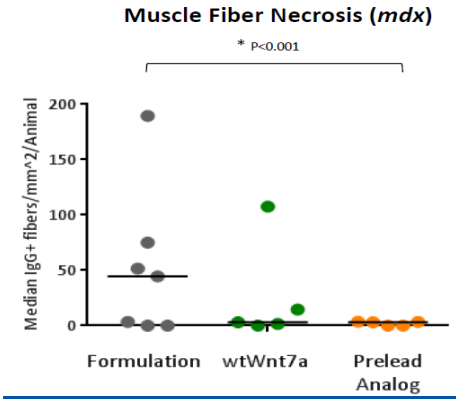
mdx mice (p<0.001). Also, there was reduction in positive staining for the CD11b marker of inflammation in muscle.

Preclinical Mouse Model: Muscle Inflammation Effect



Source: Fate Therapeutics Presentation, Fate S-1

Preclinical Mouse Model: Muscle Necrosis Effect

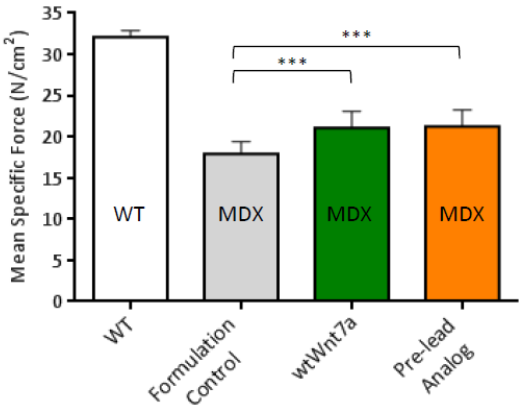


Source: Fate Therapeutics Presentation, Fate S-1

Muscle Strength: Skeletal muscle strength was also evaluated in the *mdx* mouse model. Strength was measured by specific force *(the maximum amount of active, constant force produced per muscle fiber cross-sectional area, typically measured in newtons per square centimeter (N/cm²), as muscle force is typically proportional to muscle size)*. Wild-type mice had greater muscle strength than *mdx* mice, as would be expected. Twelve *mdx* mice each were injected with a single administration of Wnt7a, Wnt7a analog, or formulation control, and strength in the tibialis anterior muscle was measured. Compared to *mdx* mice administered control, mice injected with Wnt7a and Wnt7a analog had significant increases of approximately 18% and 19%, respectively, in muscle strength measured by specific force (p=0.0002 and p=0.0001, respectively).

Preclinical Mouse Model: Skeletal Muscle Strength Effect

In Situ Force Measurements				
	WT	Formulation Control MDX	wtWNT7a MDX	Pre-Lead Analog MDX
Number of Animals	5	12	12	12
CSA (mm²)	4.99±0.50	7.67±0.68	7.02±0.52	7.26±0.70
Tetanic Force	1599±147	1372±172	1476±169	1536±167
Specific Force (N/cm²)	32.09±0.79	**17.88±1.52**	**21.03±2.04**	**21.23±1.99**
P value	<0.0001	N/A	0.0002	0.0001
Force Increase (% Control)	79.5	0	17.6%	18.7%



Source: Fate Therapeutics Presentation, Fate S-1; ***p<0.0005

What's Next for the Wnt7a Program?

Fate is currently selecting a proprietary Wnt7a analog based on efficacy, manufacturing, and formulation characteristics, with a decision expected in 4Q13. The company has indicated that in 2014, further preclinical, IND-enabling studies will be performed for efficacy and PK assessments in a canine muscular dystrophy model, as a means of evaluating Wnt7a effects in larger muscle groups. Submission of an IND for the Wnt7a analog is planned by YE14.

Phase I Trial Plan: Fate has indicated its plan to conduct Phase I trials in 2015, with data expected in 2015. An initial Phase Ia trial will be conducted in healthy volunteers for safety assessment and dose exploration. The company will also conduct a Phase Ib, placebo-controlled, multi-dose study in patients with Duchenne Muscular Dystrophy (DMD).

The Consultant's Corner: *What Does Our Consultant Think of the Wnt7a Program?*

Our consultant, a neurologist and neuroscientist specializing in genetic muscle disorders at a major academic medical institution, was *"optimistic"* about Wnt7a-based therapy and felt that *"it is possible it will work"* in DMD. Our expert indicated that Wnt signaling has an important role in muscle stem cell proliferation and considered the rationale of this therapy to be solid, since *"a lot of the problem in DMD is lack of muscle regeneration."* According to our consultant, Wnt7a may be beneficial by stimulating muscle stem cells to proliferate and differentiate, stimulating muscle regeneration and thereby producing increased muscle mass, as well as better quality muscle (more muscle fibers without inflammation and fibrosis). She acknowledged that such a therapy would not provide a cure for DMD, but remarked that it could *"change the course of the disease"* by allowing patients greater ambulatory time and potentially less dependence on ventilator assistance in late stages, which might improve survival, since a significant proportion *("about half")* of DMD patients die from respiratory failure. As our expert stated, *"it's OK even if it is not a cure"* in this disease.

Our expert pointed out the very early nature of the preclinical data which have been produced to date, and emphasized the long path from this stage to advanced clinical development and potential approval. She described the data as *"encouraging"* and remarked that the results to date *"very convincingly"* demonstrate increase in muscle mass, force, and histopathology as a result of Wnt7a administration in the mouse model. Additionally, our consultant pointed out as a very significant positive the caliber of the scientific team behind these efforts, describing the members as *"really top notch, very careful scientists…you could not ask for a better group of scientists that have developed this."*

With the caveat that it is still early, our expert predicted that, if a clinical trial demonstrates a Wnt7a therapeutic is safe, tolerable, and produces *"some improvement in ambulation,"* the drug would be approved, especially given *"the bar is incredibly low in DMD"*, with steroid therapy as the only drug with proven skeletal muscle benefit in the disease. The one significant safety concern pointed out by our consultant was the potential for a Wnt7a drug to cause or exacerbate malignancies, given its involvement in molecular proliferation signaling pathways,

and the fact that DMD treatment is long-term. Finally, our consultant had a positive view that Wnt7a therapy may also have a place more broadly in therapy for other neuromuscular disorders; *"stimulating satellite cells is going to be helpful for muscle regeneration no matter how you got to the muscle disorder."*

Duchenne Muscular Dystrophy (DMD): Brief Overview

Duchenne Muscular Dystrophy (DMD) is an X-linked genetic and fatal neuromuscular disorder affecting approximately one in 5,000 newborn boys. The disease results from mutations in the dystrophin gene (*DMD* gene), located on the short arm of the X chromosome. Female carriers usually demonstrate much milder symptoms or are asymptomatic. In rare cases, associated with chromosomal rearrangement or skewed X chromosome inactivation, affected girls can have disease severity comparable with that seen in boys.

DMD is the most common type of muscular dystrophy and the most severe form of muscular dystrophy in childhood, characterized by early onset of muscle degeneration and wasting. Progressive muscle weakness develops in early years of life, with clinical symptoms typically becoming evident between the ages of 3 and 5 years. Patients may make some progress in motor function until the ages of 4 to 6 years, but eventually lose independent ambulation, becoming paralyzed and wheel chair-bound by the early teenage years. Cardiomyopathy and respiratory difficulty usually begin by the age of 20 years, and patients typically die from respiratory failure or lung disorders by age 25 years. Cognitive dysfunction may also emerge with disease progression. Even with assisted ventilation, life expectancy is less than 30 years.

DMD Diagnosis: Most DMD patients are diagnosed around the age of five years, when clinical symptoms become evident. The DMD Care Considerations Working Group, a group of 84 clinicians selected by the US Centers for Disease Control and Prevention (CDC) to develop recommendations for DMD, has published guidelines for DMD care (Bushby K et al., *Lancet Neurology* 2010). According to these guidelines, the diagnosis of DMD should be considered, irrespective of family history, by one of the following: **1)** *(most commonly)* observation of abnormal muscle function in a male child; **2)** detection of an increase in serum creatine kinase *(an indicator of muscle damage)* tested for unrelated indications; or **3)** elevated liver transaminases, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), produced by muscle as well as liver cells. Initial symptoms may include delayed walking, frequent falls, or difficulty running and climbing stairs.

Blood testing for *DMD* mutation is always necessary. Dystrophin mutations may be identified by genetic tests, such as multiplex PCR. Once the mutation is identified and fully characterized, no further testing is necessary. Muscle biopsies can be performed, with the key diagnostic tests being immunocytochemistry and immunoblotting to detect dystrophin, which is mostly absent in DMD. Following a positive biopsy diagnosis of DMD, genetic testing is mandatory. However, a muscle biopsy is not necessary if genetic testing first establishes the diagnosis.

DMD Treatment: There are no disease-modifying treatments available for DMD. Steroid therapy (glucocorticoid) is the only medication currently available which slows decline in muscle strength and function in DMD. The DMD Care Considerations Working Group guidelines suggest consideration of glucocorticoid therapy in all DMD patients, with timing of therapy initiation being an individual decision. It is recommended that therapy not be initiated when a child is gaining motor skills, especially under age 2 years. Guidelines recommend treatment initiation once a plateau phase has been identified, usually at age 4-8 years *(no more progress in motor skills, but prior to decline)*. Furthermore, therapy even at later stages, in full decline or with marginal ambulation, is also recommended, though it is recognized benefit may be more limited. Daily steroid therapy is preferred to alternative regimens.

Competitor Agents in Development for DMD

1) Eteplirsen: Sarepta is developing the RNA-based therapeutic eteplirsen for DMD, which corrects mutations in the dystrophin gene by skipping exon 51, restoring protein production. Sarepta has conducted three clinical trials of eteplirsen. The first proof-of-concept study was conducted with intramuscular injection. A second open-label, Phase Ib/II study evaluated systemic IV administration of eteplirsen at escalating doses. The Phase IIb Study 201 (as well as extension Study 202) demonstrated statistically significant and sustained clinical benefit in ambulation, as assessed with the six minute walk test (6MWT) over 84 weeks. A total of 38 patients received eteplirsen treatment in these studies, and the majority of the patients demonstrated robust, novel dystrophin production, and there have been no reported serious AEs with drug exposure of over 1.5 years. According to Sarepta, NDA submission is planned in 1H14.

2) Ataluren: PTC Therapeutics is developing ataluren for DMD. Ataluren is an oral small molecule that corrects nonsense mutations, which produce premature stop codons and disrupt dystrophin protein production. PTC has completed a Phase IIa study in 38 nonsense mutation DMD (nmDMD) patients and a Phase IIb study that evaluated the long-term efficacy and safety of ataluren in 174 nmDMD patients. The Phase IIb trial failed to meet the primary endpoint of a statistically significant change in ambulation (the 6MWT distance from baseline) after 48 weeks. However, a retrospective, post hoc analysis of the data (using modified statistical analysis to minimize impact of outliers) demonstrated a trend toward statistical significance, with p=0.0561. Ataluren is currently being evaluated in a randomized, double-blind, placebo-controlled, Phase III trial for nmDMD with ~220 patients in the declining phase of muscle function. The primary endpoint of the trial is the clinical benefit of ataluren on ambulation, as measured with the 6MWT. Secondary endpoints include assessment of physical function and quality of life. Enrollment in the trial is ongoing, and top-line data are expected in 1H15.

Fate's Intellectual Property Estate

Fate has built and is continuing to build an IP portfolio around its **1)** HSC Modulation Platform, including ProHema, **2)** SSC modulation platform, including its Wnt7a analogs, and **3)** other technologies, such as its iPSC technology. The company has rights to 46 issued and 174 pending applications.

HSC Modulation Platform and ProHema: Fate currently owns six families of US and foreign patents and patent applications covering its HSC modulation platform. This patent portfolio includes 14 pending patent applications relating to ProHema and other therapeutic compositions of stem cell modulation process.

1) Patent and patent applications co-owned by Children's Medical Center Corporation (CMCC) and The General Hospital Corporation: Fate has exclusive rights to two families of issued patents and pending patent applications, which are co-owned by the CMCC and The General Hospital Corporation. Under these patent rights, Fate has exclusive rights to 9 issued patents and 27 pending patent applications in the US and worldwide.

US Patent # 8,168,428: Fate's patent portfolio includes issued US Patent # 8,168,428, titled "*Method to modulate hematopoietic stem cell growth*." As stated in the patent abstract, "*The present invention provides for compositions and methods for modulating hematopoietic stem cell populations by using HCS modulators, which are agents that either increase HSC numbers or decrease HSC numbers as desired by a particular indication. For example, HSC modulators found to increase HSC numbers include prostaglandin E2 (PGE2) and agents that stimulate the PGE2 pathway. Conversely, HSC modulators that prevent PGE2 synthesis decrease HSC numbers. HCS modulators may be used in vitro, in vivo, or ex vivo*." This patent covers the method for promoting HSC engraftment through the *ex vivo* modulation of HSCs and expires in 2027.

2) Patent applications licensed from Indiana University Research and Technology Corporation (IURTC): Fate also has exclusive rights to two families of patent applications from the IURTC that claim:

a) methods of enhancing HSCT procedures by altering prostaglandin activity in HSCs and progenitor cells, and

b) methods for enhancing gene transduction efficacy in stem cell gene therapy.

These applications are currently pending in US and other foreign jurisdictions, and if issued, could provide patents terms that expire in 2029 or 2030.

Valuation Methodology & Investment Risks

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Company Specific Risks

Risks to our Outperform rating on FATE shares include: 1) delays or clinical setbacks in the development of ProHema, 2) delays or setbacks in the development of the Wnt7a program, 3) the possibility of additional financings, and 4) a change in the appetite for early-stage company risk among healthcare investors.

Addendum

STOCKS MENTIONED IN IMPORTANT DISCLOSURES

Ticker	Company Name
FATE	Fate Therapeutics, Inc.

Analyst Certification

Each author of this research report hereby certifies that (i) the views expressed in the research report accurately reflect his or her personal views about any and all of the subject securities or issuers, and (ii) no part of his or her compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed in this report.

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Fate Therapeutics, Inc. has been client(s) of Cowen and Company, LLC in the past 12 months.

Cowen and Company, LLC and/or its affiliates expect to receive, or intend to seek, compensation for investment banking services in the next 3 months from Fate Therapeutics, Inc..

Fate Therapeutics, Inc. is or was in the past 12 months a client of Cowen and Company, LLC; during the past 12 months, Cowen and Company, LLC provided IB services.

Cowen and Company, LLC and/or its affiliates received in the past 12 months compensation for investment banking services from Fate Therapeutics, Inc..

Cowen and Company, LLC and/or its affiliates managed or co-managed a public offering of Fate Therapeutics, Inc. within the past twelve months.

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Cowen and Company Rating System effective May 25, 2013

Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

Market Perform (2): The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

Cowen Securities, formerly known as Dahlman Rose & Company, Rating System until May 25, 2013

Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

Sell – The fundamentals/valuations of the subject company are deteriorating and the investment return is expected to be 5 to 15 percentage points lower than the general market return

Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

COWEN AND COMPANY RATING ALLOCATION

Distribution of Ratings/Investment Banking Services (IB) as of 09/30/13

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	394	58.72%	54	13.71%
Hold (b)	255	38.00%	5	1.96%
Sell (c)	22	3.28%	1	4.55%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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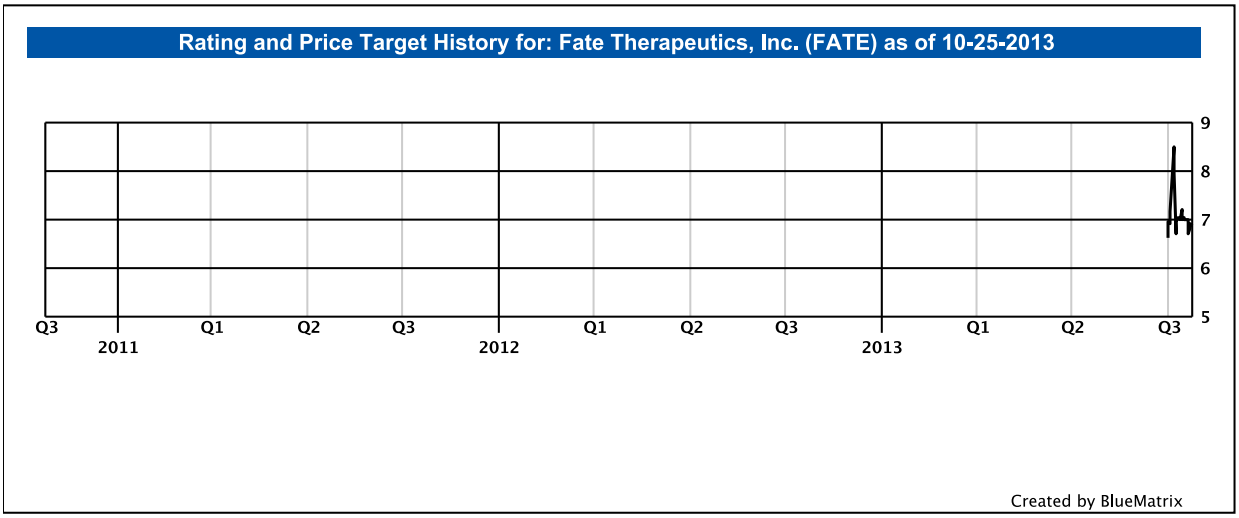

Legend for Price Chart:

I = Initation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | $xx = Price Target | NA = Not Available