Zacks Small-Cap Research

March 30, 2012
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Cytomedix, Inc (CMXI-OTC)

CMXI: Cytomedix Remains One Of Our Best Ideas In Small-Cap Biotech…

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	01/30/2011
Current Price (03/30/12)	$1.38
Target Price	**$3.00**

FULL REPORT

In mid-February 2012, Cytomedix made a bold acquisition to acquire privately-held Aldagen, Inc. for $16 million in upfront consideration, and another potential $24 million in backend milestones. Aldagen gives Cytomedix a mid-stage development pipeline focused on cardiovascular disease and a platform technology with ALDH bright cells. We see a number of synergistic opportunities between Aldagen's technology and Cytomedix' two approved medical devices. The deal creates a potential leader is regenerative medicine, and gives the new Cytomedix a strong foothold in stem cell therapeutics to be funded by the commercial success of both Angel and AutoloGel. We reiterate our 'Outperform' rating and raise our target to $3 per share.

SUMMARY DATA

52-Week High	**$1.40**
52-Week Low	**$0.28**
One-Year Return (%)	**294.29**
Beta	**1.20**
Average Daily Volume (sh)	**97,227**
Shares Outstanding (mil)	**57**
Market Capitalization ($mil)	**$79**
Short Interest Ratio (days)	**1.62**
Institutional Ownership (%)	**3**
Insider Ownership (%)	**40**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**21.7**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2012 Estimate	**N/A**
P/E using 2013 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2011	1.4 A	1.4 A	1.5 A	3.0 A	7.3 A
2012	3.8 E	3.0 E	2.1 E	2.4 E	11.3 E
2013					13.5 E
2014					26.2 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2011	-$0.03 A	-$0.02 A	-$0.04 A	$0.01 A	-$0.08 A
2012	-$0.00 E	-$0.02 E	-$0.03 E	-$0.03 E	-$0.07 E
2013					-$0.05 E
2014					$0.05 E

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WHAT'S NEW

Financial Results

On March 29, 2012, Cytomedix reported financial results for the fourth quarter and full year ended December 31, 2011. Total revenues in the fourth quarter 2011 were $2.96 million, comprised of $1.61 million in product sales and $1.35 million in partial recognition of non-refundable option fee in connection with the potential strategic supply and distribution partnership for AutoloGel U.S. chronic wound market. Product sales were made up of $1.52 million in sales of Angel, up 26% from the fourth quarter 2010 and 6% sequentially from the third quarter 2011 and $0.09 million in sales of AutoloGel, up 10% from the fourth quarter 2010 but down 10% sequentially from the third quarter 2011. Total revenues for the full year 2011 were $7.25 million, comprised of $5.90 million in product sales and $1.35 million in the non-refundable option fee noted above. Angel product sales in 2011 totaled $5.51 million, up 61% year over year. AutoloGel product sales totaled $0.39 million, up 5% year over year from 2010.

Net income for the fourth quarter 2011 was $0.81 million, or 1 cents per diluted share. This was in-line with our model. Net loss for the full year 2011 totaled $3.9 million, or 8 cents per share. Cytomedix burned approximately $4.3 million in cash in 2011. Cytomedix exited 2011 with $2.3 million in cash and equivalents and $5.2 million in current assets. The company has $3.1 million in current liabilities and $2.1 million in debt.

Expectations For 2012

We currently model total revenues in 2012 at $11.3 million, comprised of $8.1 million in products sales coming from $0.8 million in AutoloGel, $6.9 million in Angel, and $0.4 million from research products at Aldagen, and $3.2 million in recognition for the remaining non-refundable option fee from the potential strategic supply and distribution partnership on AutoloGel. We note our model assumes no additional upfront payment from the potential AutoloGel partner in 2012, despite our belief that a deal will get done in the second quarter 2012 and provide an additional modest upfront payment to Cytomedix. We model a net loss in 2012 of approximately $5.8 million, or 7 cents per share. We see a number of catalysts coming later this year. These include:

Upcoming Events	Time
Millennia Holdings to publish AutoloGel data from Japan	April 2012
Present data on AutoloGel at Advanced Wound Care symposium	April 2012
Preliminary decision from CMS on National Coverage	May 9, 2012
Finalize partnership with "Top-20 global pharma company" on AutoloGel	Mid-2012
DSMB clearance to move into part-2 of the RECOVER-stroke	Mid-2012
Roll out "peer-to-peer" webinar strategy to maximize Angel orthopedic sales	Mid-2012
File BMAC applications for EU CE Mark	Q3-2012
Decision from U.S. FDA on Angel 510(k) BMAC application	Q3-2012
File U.S. 510(k) application for "next-gen" AutoloGel 2.0 product	Q3-2012
Final decision from CMS on National Coverage	August 2012
Facilitate ISTs on PRP with Angel	2H-2012
Facilitate ISTs using ALDH-br+ cells	2H-2012
Initiate phase 2 program in CLI with ALD-301	Late 2012
Complete enrollment in RECOVER-stroke	Late 2012
Data from RECOVER-stroke	Q2-2013
U.S. FDA approval of "next-gen" AutoloGel 2.0 product	2H-2013
Enter into collaboration agreement for Phase 3 stroke trial with ALD-401	2H-2013

INVESTMENT THESIS

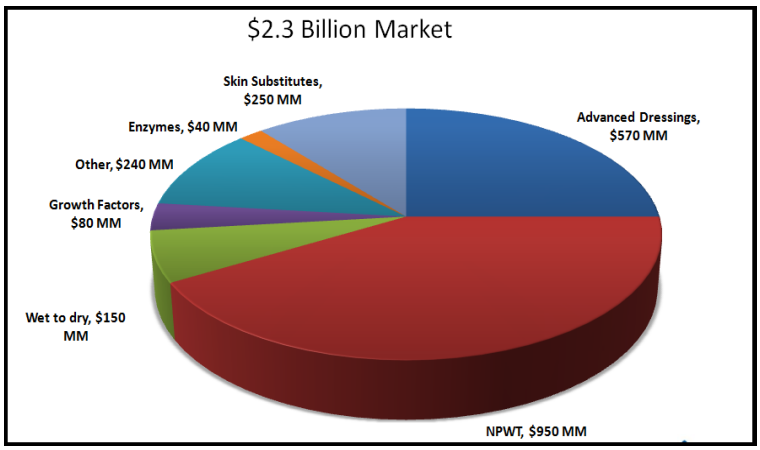
A Potential AutoloGel Partner

On February 2, 2012, Cytomedix announced that it remains in active discussion with an undisclosed "Top-20 global pharmaceutical company" seeking to license AutoloGel for distribution into the U.S. chronic wound market. We remind investors that back in October 2011, Cytomedix announced it has received a $2.0 million payment from the aforementioned undisclosed partner for the right to exclusively negotiate to distribute and promote AutoloGel in the U.S. through a dedicated, hospital-based sales force. The $2.0 million payment bought the pharmaceutical company exclusivity through the end of December 2011. In February 2012, Cytomedix received another $2.5 million to extend the exclusivity period to June 30, 2012.

According to management, the company has essentially completed their due diligence and is waiting to make an offer. We are not expecting an offer until after the CMS decision on national coverage expected on or before May 9, 2012. Any deal is expected to include a modest upfront payment – we guess $5.5 million, which would bring the total upfront payment to $10.0 million, and backend milestones and profit-sharing royalties on sales. Cytomedix noted that it expects a significant milestone on the U.S. approval and first commercial sales of the next-generation AutoloGel product (which we call AutoloGel 2.0).

…Could be Meaningful For AutoloGel Sales…

The market for products addressing chronic wounds in the U.S. is estimated to be $2.3 billion annually. There are over 6 million wounds (primarily diabetic foot ulcers, venous leg ulcers, and pressure ulcers) treated each year. Platelet rich plasma (PRP) products like AutoloGel represent only a small fraction of the market share. There are dozens of alternative therapies that compete with AutoloGel, some of them commodity types of products that have established habitual use patterns or set provider contracts to encourage standardized use.



Acceptance of new products, like AutoloGel, is generally slow. And to make things more difficult, many of the competitors are larger companies with established resources and significantly expanded sales and marketing efforts. To date, Cytomedix has been focusing its sales efforts on sub-markets with established payment pathways for AutoloGel such as long-term acute care hospitals (LTAC) and Veterans Administration (VA) facilities. The company currently has 6 part-time representatives promoting AutoloGel.

The "top-20 global pharmaceutical" partner that Cytomedix remains in partnership discussions has a hospital-based sales force of approximately 100 full-time representatives. This would be an enormous increase in promotion from Cytomedix's current 6 part-time representatives. The company also has established relationships in the biologic market and deep pockets to fund the education and awareness campaign needed to drive AutoloGel use. AutoloGel, with its outstanding clinical data and ease of use, could really benefit from this sort of tier-1 promotion. However, the biggest driver in the next few quarters is CMS reimbursement. AutoloGel sales in 2011 were only $0.39 million. National CMS coverage and tier-1 promotion from a top pharmaceutical partner could turn AutoloGel into a $50 million products in the years to come.

…It's All About Reimbursement…

The extension of the exclusivity period to June 30, 2012 is all about the National Coverage Analysis (NCA) for AutoloGel first filed in May 2011. The public comment period for the Centers for Medicare & Medicaid Services (CMS) reimbursement dossier has closed. Cytomedix recently met with CMS to discuss all 121 public comments. We have read all 121 comments. We consider 118 to be positive. The 3 negative comments were from potential competitors (Organogenesis and SafeBlood).

We expect CMS to make a preliminary decision on AutoloGel coverage on or before May 9, 2012. If positive, we would expect that the partnership will be signed shortly thereafter. CMS coverage would be a significant leap-forward for AutoloGel use. This process dates back over seven years, to when CMS first reviewed and rejected the original NCD application in 2003 based on a lack of significant evidence on safety, efficacy, and cost-effectiveness. The NCA submission in May 2011 culminates over seven years of data collection and diligent work by management to file for reconsideration.

Since the time of the filing, management has continued to work closely with the agency, holding face-to-face meetings in March and May 2011 before the filing, and just recently in January 2012 to discuss the public comments. CMS asked Cytomedix to prepare a "net health benefit" presentation as part of the filing. The agency has provided an initial review of the data and laid out its plan to provide Coverage with Evidence Development (CED). CED allows for Medicare coverage for the appropriate use of an item or service while additional data is collected to support its ongoing use for Medicare beneficiaries. It's full coverage with no restrictions or limitations. The best algology would be an "accelerated approval" or an approval with the requirement of a phase 4 (post-market) surveillance study.

As part of the filing, Cytomedix included data from 285 patients in its wound care registry. We expect that CMS will ask Cytomedix to expand this registry as part of the CED procedure. At this point, questions remain on just how many more patients and what endpoints CMS would like to see. Nevertheless, we do not believe expanding the existing registry to comply with CMS' guidance will be significantly expensive. And, the new patients that CED brings in should more than make up for the added cost of expanding the registry program. We here has already begun at Cytomedix to expand the registry program.

We believe coverage could be a meaningful driver of AutoloGel sales. There are approximately 2.0 million pressure ulcers and 1.5 million diabetic foot ulcers each year in the U.S. where AutoloGel could be an effective product. However, approximately half of these are in patients covered by Medicare / Medicaid, and non-coverage has been a significant impediment for uptake. There is virtually no government business for AutoloGel now. Instead, management has been focusing on private pay procedures, LTAC and VA hospitals as noted above, but the lack of a national coverage decision on the product has limited uptake in this area as well. CMS is the gate-keeper. CMS coverage not only kicks open the door to Medicare / Medicaid, it also meaningfully expands private pay coverage and local and state reimbursement plans as well.

…Data Supports Coverage…

Back when CMS issued its non-coverage designation for AutoloGel in 2003, the decision was based on limited information that included data from only 40 diabetic foot ulcers. Since that time, management has been able to collect data on over 500 wounds – over 10 times the data previously submitted to CMS. And, the data includes new wound types such as pressure ulcers, venous ulcers, and other surgical wounds.

Wound Data Source	**No. of Wounds**
Original Data	40
Market Registry	285
Millennia Group	100
TAPS phase 4 Study	100
New Total	**~525**

Wounds In Market Registry	**No. of Wounds**
Pressure Ulcers	142
Diabetic Ulcers	41
Venous Ulcers	32
Dehisced Wounds	24
Surgical Wounds	27
Traumatic Wounds	11
Other Wounds	8

…Net Health Benefit Evenident…

As noted above, CMS asked Cytomedix to prepare a net health benefit to the use of AutoloGel. Cytomedix recently announced publication of compelling clinical data from a wound outcomes registry in the *International Wound Journal* and published data from a comprehensive systematic review and meta-analysis (statistical pooling) of the use of PRP gel in wound healing in *ePlasty*, the open access journal of the *Journal of Plastic Surgery.* Data at SAWC in April 2011 highlighted comparing the use of platelet rich plasma (PRP) gel (AutoloGel) and negative pressure wound therapy (NPWT) in the long-term acute care setting. Results demonstrate that PRP greatly improved the wound healing outcomes while also cutting costs associated with the overall treatment. The study was conducted at the Asheville Specialty Hospital, in Asheville, NC.

Wound Healing Rates PRP vs. NPWT

			Area			Volume		
	Avg No. Days Treated	Avg No. Treatments	Total % Reduction	% Reduction/ Day	% Reduction /Week	Total % Reduction	% Reduction /Day	% Reduction /Week
PRP	7.3	1.7	27.5	1.4	**10**	54.9	11.4	**79.6**
NPWT	9.2	4.1	25.8	0.9	**6.4**	40.7	6.4	**45.1**

PRP was used fewer days and required fewer dressing changes, yet yielded faster healing rates.

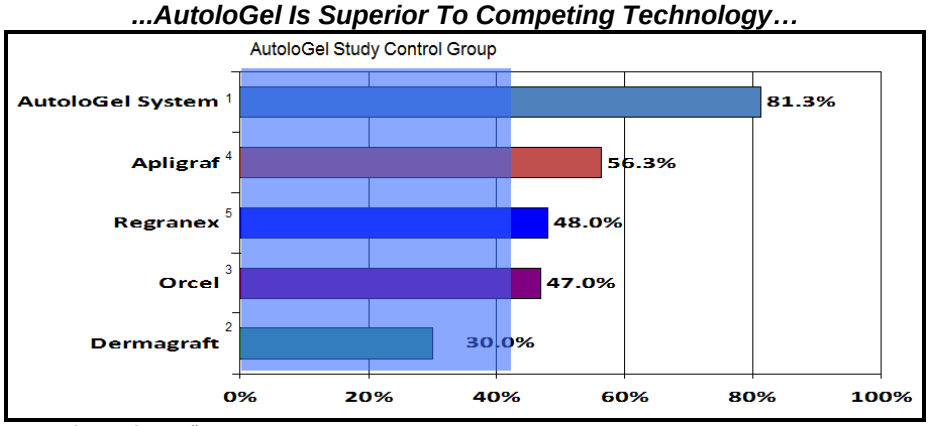
Actual (mean) cost of PRP (n=25):
➔ $11,850

Estimated (mean) cost of NPTW using historical data (n=17):
➔ $26,169

Total estimated cost savings of using PRP vs. NPTW:
➔ $14,319.

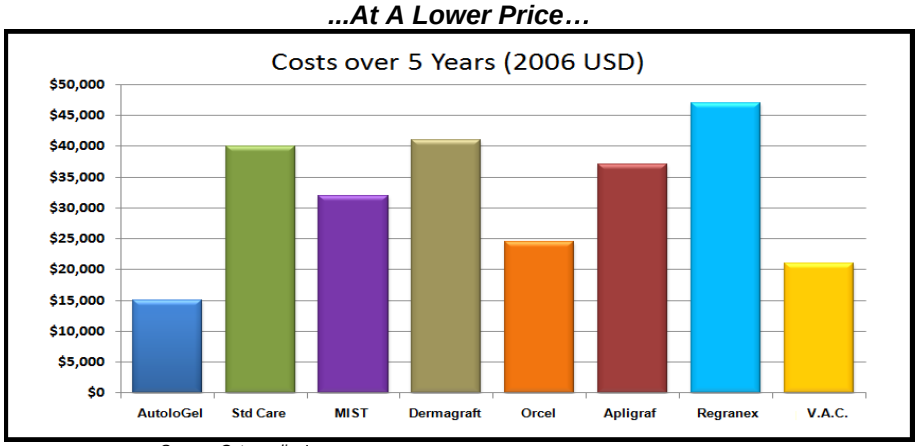
We believe this is strong data in Cytomedix favor, and exactly the kind of stuff Centers for Medicare and Medicaid Service (CMS) is looking for. Not only did AutoloGel heal patients faster and more effectively, but it also costs about 60% less than traditional treatment.

...AutoloGel Is Superior To Competing Technology…



Source: Cytomedix, Inc.

...At A Lower Price…



Source: Cytomedix, Inc.

The cost data above was collected via an independent pricing study conducted by B&D Consulting in September 2007. B&D is an independent advisory and advocacy firm located in Washington. The firm completed a cost effectiveness analysis of AutoloGel compared to alternative therapies for patients with diabetic foot ulcers. Results of this study demonstrate AutoloGel offers a lower cost and better healing outcomes than the other therapies analyzed. According to B&D's findings, the estimated 5-year average direct wound care costs (exclusive of lost work, disability, etc.; inclusive of recurrent wounds, amputations) when AutoloGel was used to treat the most commonly sized diabetic foot ulcers were approximately $15,000. This compared very favorably to alternative therapies ranging from $24,000 to $47,000, including standard of care (gauze / advanced dressings) at $40,000. B&D's work also suggests a measurable increase in Quality Adjusted Life Years (a function of increased survival rates and fewer wound complications) with AutoloGel.

This study was published in the journal Advances in Skin and Wound Care in December 2008. Prior to the publishing of this paper, CMS would not consider this data as part of the reconsideration package. However, now that the data has been published for peer-review, Cytomedix did include it as part of the CMS dossier. We believe when price is factored into the equation the product becomes even more impressive.

…Data From Japan…

In September 2009, Cytomedix entered into a license and distribution agreement with Millennia Holdings, Inc., a contract service organization that operates approximately 22 wound care centers and hospitals across Japan, along with a home care division. Millennia has been collecting data from roughly 160 patients (>200 wounds) designed to orchestrate regulatory approval in Japan. Millennia is on track to complete its studies this year. In fact, initial data from Millennia will be published in the April issue of Ostomy Wound Management. Cytomedix expects to secure a distribution agreement in Japan, with Millennia or one of Millennia's partners, around the regulatory approval.

…Hair Restoration & Plastic Surgery…

CMS coverage is clearly important to the future of AutoloGel, but we note that management is making inroads into the private pay market with AutoloGel was well. In June 2011, Cytomedix launched AutoloGel into the hair restoration market and in July 2011 management held a webinar for specialty plastic surgeons that generated strong product interest. In September 2011, management will have an exhibit at the annual meeting of the International Society of Hair Restoration Surgery, where hair restoration specialist, Dr. Robert J. Reese, will moderate a panel discussion on the use of physiologically relevant concentrations of platelet rich plasma (PRP) in hair restoration surgery. Management plans to use this promotion, along with other efforts, to drive sales of AutoloGel in this new market opportunity. So far the feedback has been outstanding. The good thing about the private pay market is it is not subject to national coverage or CMS reimbursement issues.

…510(k) on AutoloGel 2.0 Later In 2012…

Cytomedix is working to bring an enhanced next-generation AutoloGel – AutoloGel 2.0 – to the market. The company has been working with bioengineers to develop a simplified and more cost-effective product. AutoloGel 2.0 employs optimized technology through changes to the centrifuge and the design of a new separation device that operates in a semi-closed system where the blood will be drawn directly into the device, removing any margin for error and providing for much better management of the waste material. This streamlines the process making the clinical procedure more efficient, especially in orthopedic indications.

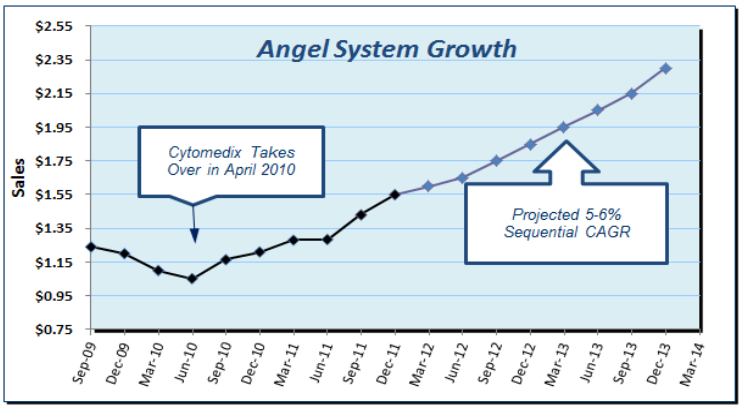
The sterilization studies are complete. Management is currently working on the platelet characterization and validation studies. We are expecting the 510(k) for AutoloGel 2.0 in the third quarter 2012. We believe management is also waiting for the preliminary decision from CMS before they proceed with the application. If CMS reimbursement is established, we expect management to move quickly with the 510(k) filing after the validation work has been completed. The new version should improve the company's intellectual property protection around AutoloGel and deliver enhanced profitability for the future.

As noted above, Cytomedix expects that any deal for AutoloGel signed with the pharmaceutical partner will tie in significant development and commercialization milestones around AutoloGel 2.0.

Angel Just Getting Started

Angel sales were slightly above expectations in the fourth quarter 2011, coming in at $1.52 million vs. our estimate of $1.50 million. Sales were up 26% year-over-year and 6% sequentially. Sales in 2011 were $5.51 million, up 61%.

The trajectory looks fantastic since Cytomedix took over full Angel promotion in April 2010. We model $6.85 million in Angel sales in 2012.



We believe a significant opportunity exists for management to expand use of the device at the smaller perfusionist practices where Angel system utilization is low. This will be a core area of focus for management in the coming quarters. In the meantime, customer retention remains high. Over 95% of the revenues are from the U.S., and 80% of those are from the single-use consumable sets sold for the system. Cytomedix acquired Angel with 180 systems installed. Since that time, management has been able to add another 100 systems into the market.

Cytomedix is looking to expand its distribution network in Europe. In February 2011, Cytomedix received CE Mark certification for Angel and ActivAT throughout the 28 country European Economic Area (EEA). This finalized the transfer outside the U.S from Sorin. Cytomedix continues to build out its sales infrastructure. The company employs 6 regional sales managers and 20 independent agents. We expect management to add 6 to 8 new sales managers and field reps in the coming year. The number of independent reps has grown each quarter as Cytomedix expands its network to promote Angel.

…New Indications to Drive Growth…

Management has been making some headway with expanding the Angel market opportunity into cardiovascular indications and orthopedics. CEO Martin Rosendale recently highlighted the potential for new indications for the Angel system. These include bone marrow aspirate processing (BMAC), blood reinfusion during surgery, and expanding uses of the device in the orthopedic / sports medicine market.

BMAC: On September 1, 2011, Cytomedix announced that it had filed a 510(k) application to the U.S. FDA for use of the Angel Whole Blood Separation System for the processing of bone marrow aspirate. The expanded indication includes processing a mixture of blood and bone marrow, a rich source of stem cells, to create a bone marrow aspirate concentrate (BMAC). *In vitro p*erformance testing with Angel yielded statistically significant improvement in the concentrations of hematopoietic progenitor / stem cells, reduced presence of pro-inflammatory cells, and provided better separation of platelet rich plasma (PRP) and red blood cells compared to alternative devices.

Angel has the potential to deliver RPR with highly viable bone marrow stems cells in a real-time, point-of-care setting for use in orthopedic or cardiovascular indications. There are approximately 500,000 spinal fusion procedures performed each year and the application of bone marrow or bone marrow concentrates has been the historical gold standard to support effective fusion. The biologics market associated with spinal fusion procedures is approximately $800 million annually. We note that some clinicians are already successfully using Angel in this indication today. However, FDA clearance will allow Cytomedix to market the Angel System for this significant opportunity. The ease-of-use, separation efficiencies, and high quality output, are of notable benefit and competitive advantage compared with other commercially available systems. We are expecting a decision back from the U.S. FDA on the 510(k) application in the third quarter 2012.

Reinfusion: Before Cytomedix took over, Sorin was already seeing real-world use of the Angel device during surgery for total blood management. Cytomedix is looking to file a 510(k) application to expand the label to include the reinfusion of packed red blood cells separated during the bone marrow processing procedure. The company needs to conduct a small human study prior to filing the 510(k). We think this opens the door for potential use in the surgical setting by cardiologists potentially for initiations such as critical leg ischemia (CLI). If Angel can deliver real-time highly viable stem cells along with PRP, this could be an enormous revenue opportunity for Cytomedix. We note that some clinicians are already successfully using Angel in this indication today. Cytomedix plans to help facilitate investigator sponsored trials (ISTs) in this area later this year.

This is where a potential marriage of Angel and Aldagen gets interesting. We see synergies in the manufacturing debulking progress and the potential for Angel's PRP (or even platelet poor plasma) to be used as the delivery vehicle for ALD-201 or ALD-301. Angel separates the red blood cells in as little as fifteen minutes. Incorporating Angel into Aldagen's process could save four hours on the processing time. And using AutoloGel to treat chronic wounds in patients with CLI could improve the outcome of the trial when used with ALDH^{br} Cells.

Aesthetic Applications: Angel is being used in the U.K. for aesthetic applications, where physicians are injecting PRP under the skin to facilitate skin rejuvenation. Angel PRP is also being used in fat transfer procedures to improve graft survival and aesthetic outcomes. These innovative applications represent development opportunities for future Angel indications. It places Angel squarely in competition with Cytori's PureGraft and Celgraft products for these aesthetic and plastic surgery market.

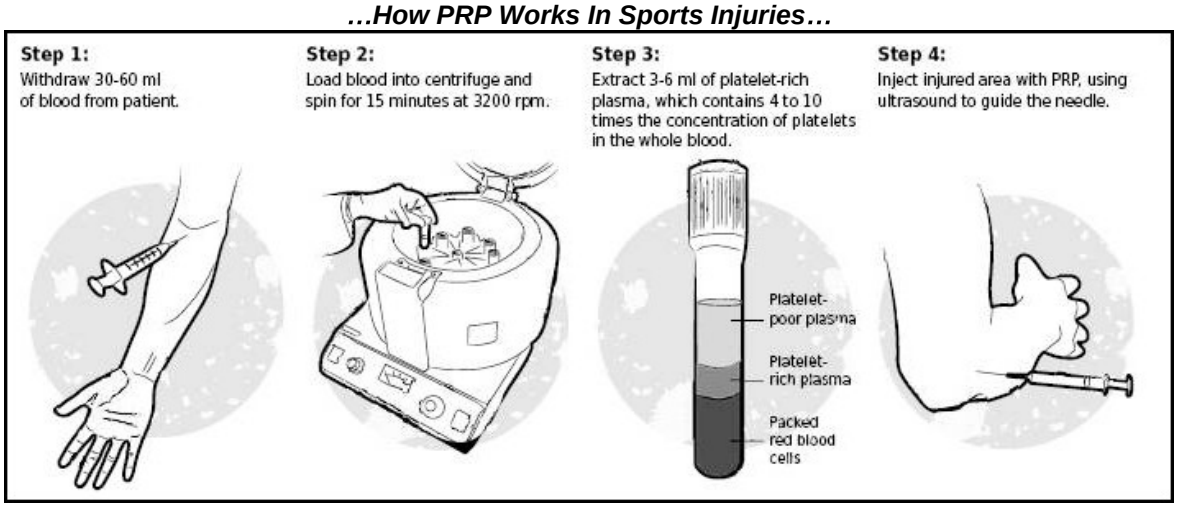
Sports Medicine: Sports medicine remains the "Holy Grail" for Angel. Evidence that using PRP to shorten and improve healing with knee, ankle, elbow, or an ACL or MCL sprains is growing rapidly. We have seen clinical data demonstrating PRP is effective at treating chronic tennis elbow, severe Achilles tendonitis and osteoarthritis of the knee. Tiger Woods was reported to use PRP to shorten his recovery time after his ACL tear in 2008. Pittsburgh Steelers' Hines Ward and Troy Polamalu both used PRP to recover from an injury during the 2008 NFL season in which the team won the Super Bowl. The use of PRP is clearly on the rise in professional sports. The LA Dodgers, Seattle Mariners, Denver Nuggets, NY Mets, and Dallas Cowboys have all embraced the use of PRP. In fact, we are now beginning to see use in college and amateur athletics. Standards have yet to be set however, and some sports purists are bringing up ethical questions regarding the use of PRP. In fact, the World Anti-Doping Agency, as of January 1, 2010, has banned the use of PRP in international competition when injected directly into muscle. The agency continues to allow PRP use for tendon, bone, and ligament injuries. Nevertheless, for the non-professional athlete, PRP could represent a cheap and quick alternative to a lengthy recovery processes following orthopedic surgery or a minor injury such as a muscle sprain or strain.

In the next few months we expect Cytomedix to see additional data on the use of PRP in treating sports injuries. Cytomedix is working with Dr. Peter H. Edwards, Jr, a board certified orthopedic surgeon with a fellowship trained specialty in Sports Medicine. Dr. Edwards practice has an emphasis on arthroscopic surgery of the knee and sports injuries of the lower extremity. He is a team physician for the U.S. Men's and Women's National Soccer Teams. Dr. Edwards has amassed data from roughly 60 patients with Achilles tendonitis, and plans to present the data at an upcoming medical meeting.

Cytomedix is also working with an Angel customer in the Northeast that plans to look at the use of PRP in 20 patients with plantar fasciitis. We view teaming up with cutting-edge physicians like this as key to the company's strategy to grow Angel in this potentially enormous market opportunity. We think the product offers doctors and trainers excellent characteristics, including improved processing time, greater sterility, and enhanced administration.

Cytomedix plans to use peer-to-peer networking and webinars to help drive use of the Angel device in orthopedics / sports medicine. As noted above, we see this as the "Holy Grail" for Angel.

…How PRP Works In Sports Injuries…



Source: Jenny Vrentas & Michael Guillen, Star Ledger

…A Little Background On Angel…

In April 2010, Cytomedix acquired the Angel Whole Blood Separation System from Sorin Group. Angel gives Cytomedix one of the leading products on the market today for platelet rich plasma (PRP) preparation, and a direct entry into the surgical market. Angel was cleared by the U.S. FDA in August 2005 and posted worldwide sales in 2010 of roughly $4.6 million (90% in the U.S.), down slightly from $4.8 million posted in 2009. Angel is a closed system that maintains aseptic conditions critical for the surgical setting. The device processes greater volumes of blood, allowing for lots between 40ml and 180 ml of four-to-six fold increased platelet rich plasma. The system is also very user-friendly, with a Microsoft Windows based operating platform, easy one button push to start, continuous volume counting and monitoring, self-loading pumps, and pre-assembled consumable (disposable) packets for fast and safe use.

The Angel System



Orthopedic surgeons are a significant user of PRP for common procedures including rotator cuff repairs, knee ligament reconstruction, meniscal repairs, ACL reconstructions, Achilles and patellar tendon repairs, and chronic tendinopathy such as “tennis elbow”. The benefits of PRP include enhanced and shorter recovery times, reduction in bleeding and pain, and reduction in infection. Thus, the sports medicine avenue for future PRP use is significant in our view. Finally, cardiovascular surgeons also use PRP to improve healing times and reduce bleeding risk during open heart surgery. Yet, despite the fact that PRP separation and concentration is an exact science, there exists on the market today dozens of approved devices to prepare PRP.

The current size of the PRP surgical market is approximately $40 to 50 million. We estimate that Angel holds around 12% market share. No one product has over 30% share; so at this point things remains wide open. Angel has certain advantages that should lead to share gains in the future. The product is built on the tried-and-true apheresis technology surgeons are familiar and comfortable with. Plus, the system is completely closed (aseptic), able to handle larger volumes than competitors, and fully customizable. However, we do not believe this is only a market share grab play. The opportunity is significant because the entire market is growing at over 20% CAGR. The company’s efforts are focused on pursuing independent arrangements aggressively to drive sales. It provides a low-cost opportunity to develop annuity-like revenues in the future through a “razor / razor blade” business model.

The economics of the product are very strong. We estimate gross margins on the disposable device is >70%, and with only about 240 installed units (systems) the majority (~90%) of the sales are re-orders of the single-use consumable device. The centrifugation unit costs an estimated $7,500 and a single consumerable runs about $150 in the U.S. and about €160 in the E.U. Over 90% of the manufacturing is outsourced and Cytomedix has assumed these OEM agreements.

Cytomedix Acquires Privately-Held Aldagen, Inc.

On February 8, 2012, Cytomedix announced it had closed a transaction to acquire privately-held Aldagen, Inc. for 135,398 shares of Series-E preferred stock. Based on the conversion ratio into common stock and the transaction price of $1.18 per share, the deal is valued at approximately $16 million in upfront consideration. Cytomedix will also make available 20.3 million shares of common stock in the form of three contingent milestone payments to existing Aldagen shareholders, as outlined below:

- 1.015 million shares (5% of the outstanding consideration) payable upon enrollment of 60 patients in the company's current phase 2 clinical trial, dubbed RECOVER-stroke, testing ALD-401 in the treatment of post-acute ischemic stroke, and final determination by the Data and Safety Monitoring Board (DSMD) that the trial may continue on plan.

- 3.046 million shares (15% of the outstanding consideration) payable upon full enrollment (100 patients) in the phase 2 RECOVER trial, if completed by May 31, 2013. If full enrollment is not reached by May 31, 2013, Aldagen can still earn half of the milestone payment (1.523 million shares) if it is completed by November 30, 2013, or one-sixth of the payment (0.507 million shares) upon successful enrollment of all patients by any time after November 30, 2013.

- 16.248 million shares (80% of the outstanding consideration) payable upon a successful outcome in the aforementioned phase 2 RECOVER program with ALD-401. A successful outcome is defined as:

    - ✓ Determination by the majority of the Board of Directors that ALD-401 has generated a positive efficacy signal defined as separation of the primary efficacy endpoint and that the data is sufficient to prepare and submit a protocol to the FDA for an adequately powered pivotal phase 3 program with ALD-401.

    - ✓ Conclusion of a successful end of phase 2 meeting with the FDA whereby the FDA determines there are no material impediments to preparing to proceed into a pivotal phase 3 program with ALD-401, or fast track approval of ALD-401 without the need for a phase 3 trial.

…A Little Financial Management Goes A Long Way…

We estimate the cost of the phase 2 RECOVER-stoke trial, along with funding operations at Aldagen, including manufacturing and overhead of the Durham, NC facility, will cost roughly $13 million through year end 2013. To help fund these costs, Cytomedix sold 4.231 million shares of common stock (at $1.18/share) to exiting Aldagen shareholders to raise $5.0 million in cash. That's right, existing Aldagen shareholders are funding a good chunk of the ongoing study. Cytomedix also convinced existing warrant holders of Cytomedix common stock to exercise in-the-money warrants to raise an additional $3.0 million in cash. This was done through approximately 5.7 million shares with an average exercise price of $0.50 to $0.54 per share.

This new $8.0 million in cash, along with the $2.5 million option exclusivity extension from the company's continued negotiations with a global pharmaceutical partner on AutoloGel, brings the total newly raised cash in February 2012 to $10.5 million. Cytomedix also issues 3.3 million warrants (2.115 million to Aldagen shareholders and 1.180 million to the shareholders that participated in the $3.0 million warrant exercise) at $1.42 per share as part of the transaction. Future exercising of these warrants could bring in an additional $4.7 million in cash. However, it is safe to say that management is betting on a favorable reimbursement decision out of CMS in May 2012, and an upfront payment from the undisclosed pharmaceutical partner for U.S. AutoloGel distribution rights to help fund operations over the next eighteen months. As noted above, our best guess for an upfront payment out of the pharma partner for AutoloGel following a favorable decision out of CMS is $5.5 million.

…Merging The Two Companies…

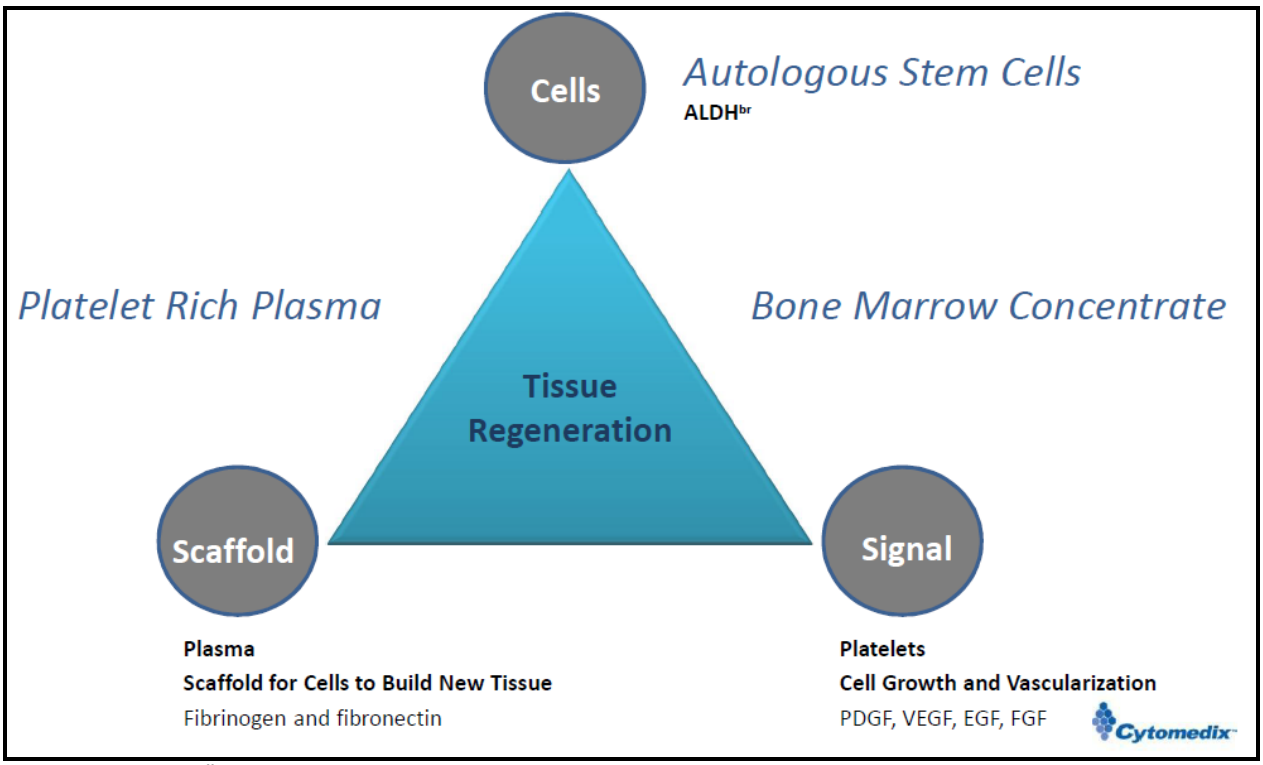
Besides ALD-401, currently in phase 2 trials for post-acute ischemic stroke, Cytomedix acquires Aldagen's proprietary stem cell technology, ALDH bright cells, and two other clinical stage candidates, ALD-301 for critical limb ischemia and ALD-201 for myocardial ischemia, along with preclinical and investigator-sponsored programs in cardiovascular disease. The pipeline includes six approved INDs by the U.S. FDA and a GMP-compliant manufacturing facility located in Durham, NC.

Edward L. Field, Aldagen's Chief Operating Officer (COO) since November 2004, will join Cytomedix as the company's new COO. Mr. Field will remain in Durham, NC. Prior to joining Aldagen, Mr. Field was the President and CEO of Inologic, Inc., a private biopharmaceutical company, from 2002 to September 2004. Prior to joining Inologic, from 1999 to 2002, Mr. Field was the President of Molecumetics, Ltd., a drug discovery and development subsidiary of Tredegar Corporation, until its merger with Therics, LLC, a regenerative medicine company. Mr. Field received a Master of Business Administration degree from the University of Virginia and a Bachelor of Arts degree in Economics from Duke University. Besides Mr. Field, another 13 Aldagen employees will join Cytomedix full-time, including Jim Hinson, Aldagen's Chief Medical Officer since July 2009. Dr. Hinson will remain as acting CMO of the Aldagen subsidiary in a consultant role.

Cytomedix also increased the size of its Board of Directors to nine (up from seven). Three new members will join the Board, including Richard S. Kent, Lyla A. Hohnke, and Joseph Del Guercio. Dr. Kent previously served on Aldagen's Board and is a partner in Intersouth Partners, a venture capital firm that was Aldagen's largest shareholder. Dr. Hohnke previously served as Aldagen's President and CEO. Mr. Del Guercio is the Managing Director at CNF Investments / Clark Enterprises, an Aldagen investor since November 2004. In early February 2012, David E. Jorden, the company's Executive Director, was appointed to Executive Chairman. James Benson, the former Acting Chairman will assume the position of Principal Director.

…Three Pillars Of Regenerative Meds…

Merging Aldagen and Cytomedix leads current Cytomedix CEO, Martin Rosendale, to believe that the company now has all three pillars of regeneration – Scaffolds, Cells, and Signals. The merger creates a leadership position in autologous regenerative medicine, with AutoloGel, Angel, and now ALDH^{br} Cells. Cytomedix plans to develop Aldagen's promising therapeutic pipeline through sales of its commercially available products – AutoloGel and Angel – along with forming partnerships and key strategic relationships around all three pillars. Cytomedix believes there are synergies in vascular disease. We remind investors that Cytomedix has filed a 510(k) application for Angel for a bone marrow aspirate indication that includes processing a mixture of blood and bone marrow. Management believes that potential synergies exist between the core products, including potentially using platelet rich (or poor) plasma as a delivery for ALDH^{br} Cells or to reduce manufacturing (debulking) by incorporating the Angel device into the Aldagen process.



Source: Cytomedix, Inc.

Aldagen, Inc. – Developing Regenerative Cell Therapies In The Cardiovascular Area

Aldagen is a clinical-stage biopharmaceutical company developing proprietary regenerative cell therapies. Product candidates consist of a specific population of a patient's own stem cells, which are isolated using our proprietary technology believed to have the potential to promote the regeneration of multiple types of cells and tissues, including angiogenesis (the growth of new blood vessels).

…ALDH Bright Cell Technology…

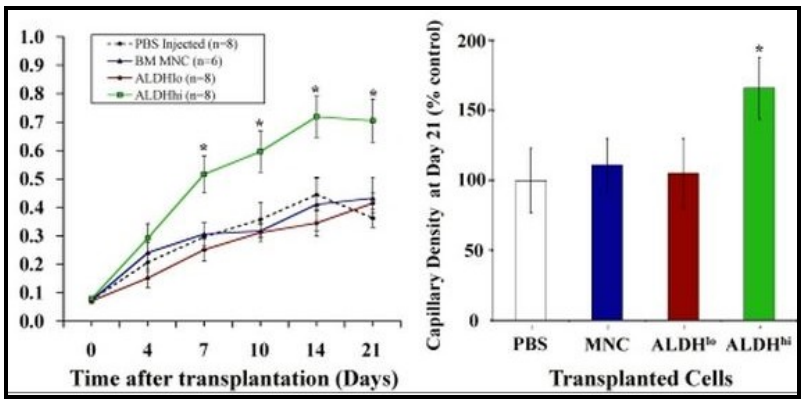
Aldagen's proprietary technology represents a novel approach to isolating specific adult stem cells for therapy. The technology licenses several patents and patent applications from Duke University and Johns Hopkins University. The technology is designed to select and isolate specific adult stem cells that express high levels of the enzyme, aldehyde dehydrogenase (ALDH). ALDH is an enzyme responsible for the oxidation of aldehydes to carboxylic acids, which leave the liver and are metabolized by the body's muscle and heart. ALDH plays an important role in controlling the developmental state of stem and progenitor cells. It converts Vitamin A into retinoic acids, which are molecules that regulate genes and influence the differentiation of blood, neural, endothelial and other types of stem and progenitor cells. Preclinical studies demonstrate that ALDH rich cells, or ALDH "bright cells" ($ALDH^{br}$ Cells), have the ability to promote angiogenesis and improve vascular function. The company has published significant research, over 250 publications, on the ability of $ALDH^{br}$ Cells to facilitate ischemic repair.

Key findings conclude that $ALDH^{br}$ Cells specifically migrate to sites of ischemic damage and induce the formation of new blood vessels at those sites. The Paracrine Effect is the release of paracrine signaling molecules at ischemic sites that drives tissue regeneration (angiogenesis and neovascularization) enhanced by $ALDH^{br}$ Cells. Other important research has been published and presented at medical meetings:

- A paper published in Congestive Heart Failure, 2009;Aug;15(4):202-6: *Bone marrow-derived aldehyde dehydrogenase-bright stem and progenitor cells of ischemic repair*, concluded that Aldehyde dehydrogenase (ALDH)-bright populations isolated from bone marrow contain potent stem and progenitor cells representing all cell types thought to be needed for ischemic repair and include hematopoietic, endothelial, mesenchymal, and neural progenitor cells.

- An poster presented at the American Society of Hematology meeting in November 2007 (Abstract #3716): *Aldehyde Dehydrogenase-Activity Purifies Multiple Hemangiogenic Lineages That Accelerate Vascularization of Ischemic Tissue through Paracrine Support of Neovessel Formation*, shows that ALDH(hi) cells possess significantly enhanced hematopoietic, endothelial, and mesenchymal stromal functions in vitro compared to unfractionated bone marrow cells.

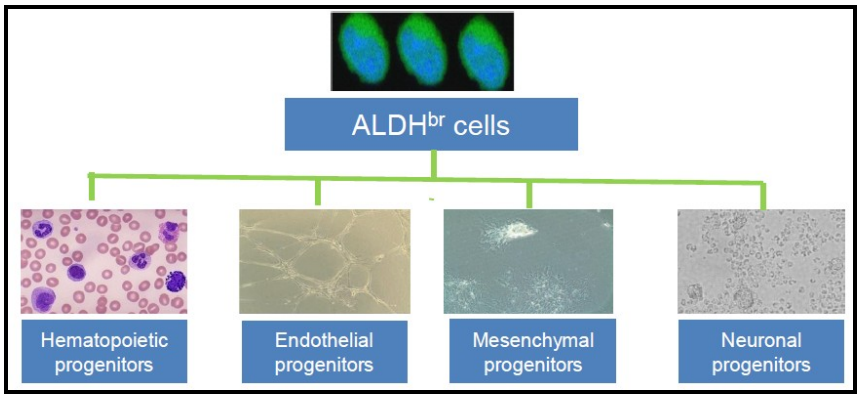
- A paper published in Blood, 2009,May:113(21):5340-51: *Revascularization of ischemic limbs after transplantation of human bone marrow cells with high aldehyde dehydrogenase activity*, concluded that human bone marrow ALDH(hi) cells improved perfusion in ischemic limbs after transplantation versus a control, bone marrow alone or bone marrow with ALDH(lo) cells.



- A paper published in Journal of Cellular and Molecular Medicine, 2011,Jan;15(1):119-33: *Aldehyde dehydrogenase activity promotes survival of human muscle precursor cells,* notes that high ALDH activity correlates to improved cell viability when human myoblasts were transplanted into host muscle of immune deficient scid mice.

ALDH^{br} Cells are a comprised of a heterogeneous cell population with multiple mechanisms of action. Gene expression studies performed demonstrating that bone marrow ALDH^{br} Cells were found to express 69 of 84 angiogenic factors tested. The 25 most highly expressed genes included soluble cytokines and growth factors, cytokine receptors, extracellular matrix proteins, and cell-cell signaling receptors. Transwell studies demonstrated that ALDH^{br} Cells responded to hypoxic conditions and to factors released from human endothelial vein cells (HUVEC) with changes in expression of specific angiogenic factors. Soluble factors released from ALDH^{br} Cells in transwell cultures under hypoxic conditions stabilized endothelial tubules formed by HUVEC. The results are consistent with the hypothesis that human bone marrow ALDH^{br} Cells can promote angiogenesis in ischemic tissues of patients with cardiovascular disease by several mechanisms including the release of soluble mediators (Journal of Stem Cell Research & Therapy, 2011,10.4172/2157-7633. Characteristics include:

- ✓ Migrate to localized ischemia.
- ✓ Produce angiogenic factors capable of improving blood flow.
- ✓ Produce neurogenic factors capable of neural repair / regeneration.
- ✓ Facilitate and achieve functional benefit.



ALDH^{br} Cells represent a very small fraction, typically less than 1%, of all cells in bone marrow. To identify ALDH^{br} Cells, Aldagen uses a proprietary chemical compound that accumulates in cells with high ALDH levels and causes these cells to emit a green florescence that can be detected by a cell sorting device. Aldagen has developed AldeFluor, a research use only (RUO) fluorescent reagent system that offers a novel approach to identify, evaluate, and isolate stem and progenitor cells based on their expression of ALDH. The company has also developed AldeCount for *in vitro* diagnostic use. Aldagen generates revenues by the sale of AldeFluor (approved in 2003) and AldeCount (approved in 2004) through a third-party distributor. The company has generated, cumulatively, about $2 million in revenues through this third-party distributor agreement. Gross margin on these products are in the ~60% range. Going forward, we do not see third-party sales of either product as a meaningful driver for Cytomedix.

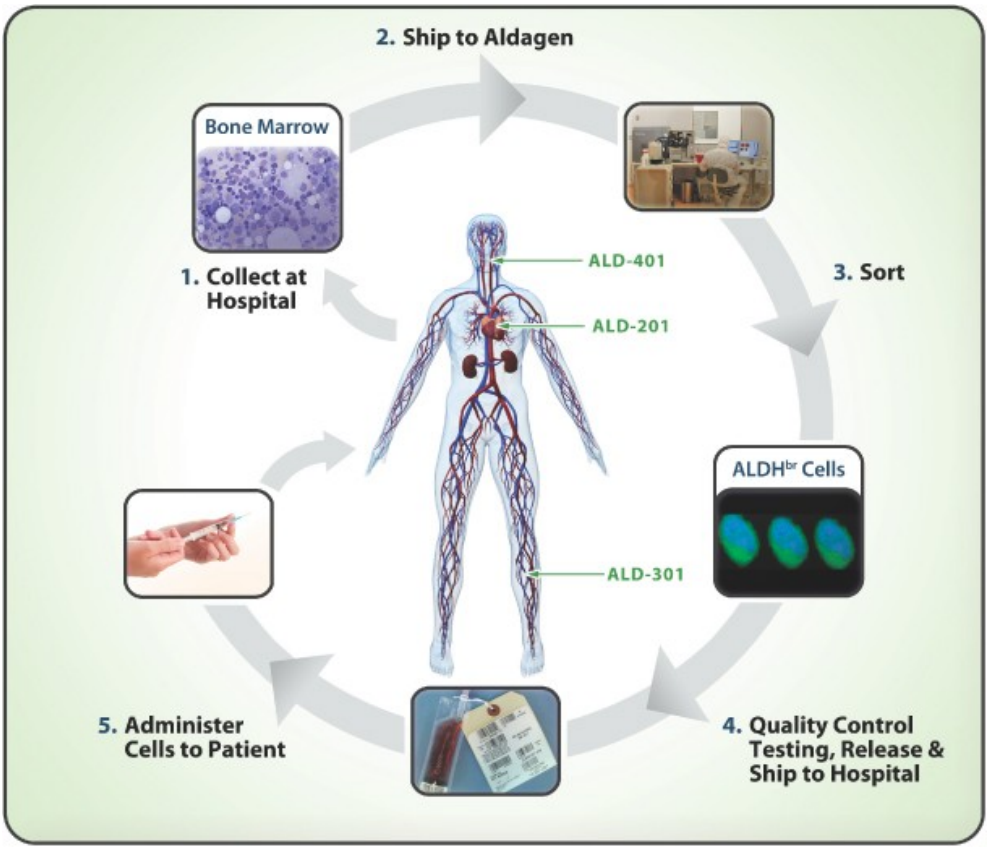
…Aldagen's Process…

Steps 1-2: Similar to other autologous stem cell therapy companies, Aldagen's process starts with a bone marrow aspiration procedure done at the hospital. A small amount (~150 milliliters) of bone marrow fluid and cells are removed through a needle put into the bone. The procedure is done on an out-patient basis and takes as little as ten minutes. The bone marrow aspirate is then shipped to Aldagen's facility in Durham, NC.

Steps 3-4: The cells are sorted and isolated using the company's proprietary fluorescent reagent compound designed to identify ALDH^{br} Cells. During this process the company conducts quality control and packaging to send back to the patient. The process takes approximately 36 hours.

There are no required manipulations, culturing or addition of growth factors to the cells. We believe this significantly reduces the manufacturing and regulatory risk, as well as costs and delay treatment of the patient. By comparison, Aastrom Bio takes 13 days to cultivate and expand its autologous stem cell therapy, Ixmyelocel-T, currently ready to enter phase 3 trials for "no option" Critical Limb Ischemia (CLI).

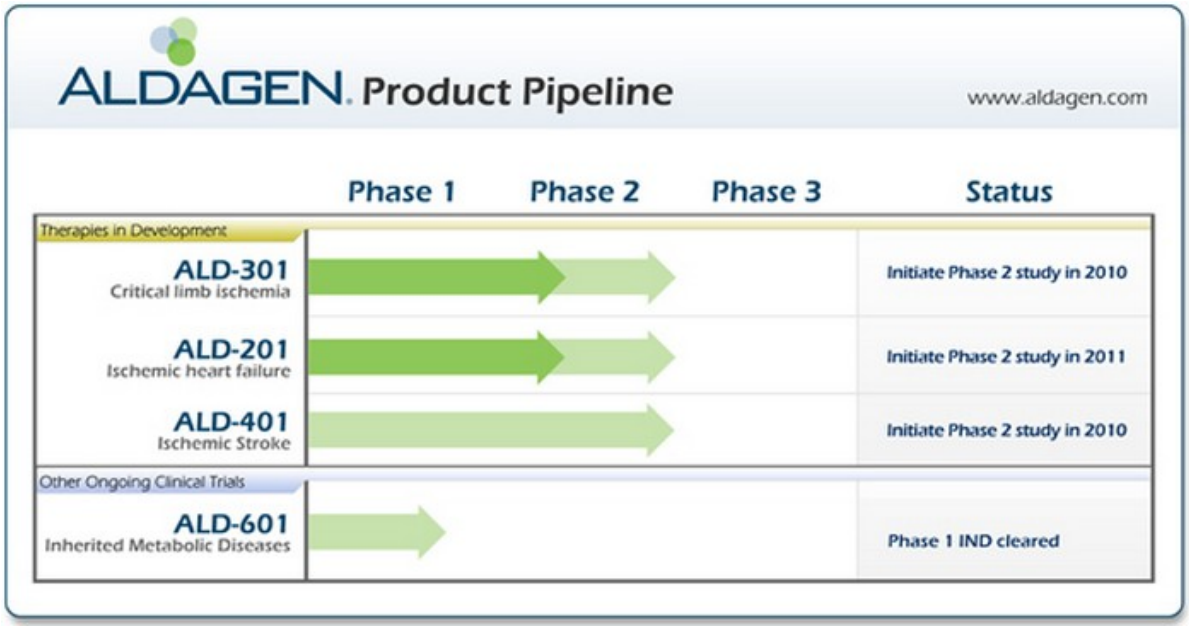
& Step 5: The ALDH^{br} Cells are administered back to the patient, either into the leg for CLI, the carotid artery for ischemic stroke, or directly into the heart for myocardial ischemia.



Source: Aldagen, Inc.

…Aldagen's Pipeline…

Aldagen has three clinical stage candidates under internal development and two candidates under investigator-sponsored programs. The company's internal focus is on developing product candidates to address cardiovascular disease. Cardiovascular product candidates are ALD-301 for the treatment of critical limb ischemia (CLI), ALD-201 for the treatment of ischemic heart failure, and ALD-401 for the post-acute treatment of ischemic stroke.



ALD-201 – Ischemic Heart Failure



ALD-201 is a formulation of ALDH^{br} Cells designed to treat ischemic heart failure. Ischemic heart failure is the result of poorly functioning heart muscle caused by reduced blood supply. In the U.S., there are an estimated 3.5 million patients with ischemic heart failure. An estimated 200,000 to 300,000 patients have no option for revascularization and are in need of a heart transplant. Unfortunately, there are only an estimated 4,000 heart transplants done annually worldwide. In the U.S., there are roughly 2,000 heart transplants done each year (Source: National Organ Procurement and Transplantation Network). That leaves an astonishing 99% of severe heart failure patients attempting to manage their disease with pharmaceutical or medical interventions. There are an estimated 1.2 million hospitalizations in the U.S. each year for acute heart failure. Clearly pharmaceutical products and medical devices are not getting the job done effectively.

Aldagen conducted a 20-patient phase 1 clinical trial with ALD-201 in 2008. ALD-201 or placebo was injected directly into the heart via a catheter delivery system (J&J's NOGA XP Cardiac Navigation System or Biosense Webster's MyoStar). Patients were followed for a total of twelve months, with an efficacy analysis after the first six months. Patients on placebo were given the option to crossover and receive an injection of ALD-201 after the first six months of the study. The primary objective of the phase 1 study was safety. Results show that ALD-201 was generally well-tolerated. However, there were some reported events worth noting:

- During the initial six-month post-treatment evaluation period, there was one serious adverse event. A patient receiving ALD-201 suffered an acute myocardial infarction (AMI). However, the AMI did not occur near the time of ALD-201 injection, and investigators determined it was unrelated to treatment.

- Among the patients who had been injected with placebo, one experienced a ventricular arrhythmia and one experienced a ventricular tachycardia. Both the ventricular arrhythmia and the ventricular tachycardia experienced by patients in the placebo group occurred during, and were considered to be related to, the NOGA mapping procedure used in the trial.

- After the initial six-month evaluation period, serious adverse events included two patients treated with ALD-201 who experienced ventricular tachycardia, in each case more than 200 days after treatment. An independent data safety monitoring board characterized the events as possibly related to treatment.

- In addition, one patient who elected to switch from the placebo group to the ALD-201 group after the initial six-month period experienced a serious adverse event of embolic stroke approximately 200 days after treatment with placebo and two days after crossover treatment with ALD-201, which the investigator determined was possibly related to the treatment with ALD-201 or the NOGA mapping procedure.

Secondary endpoints included efficacy measures such as aerobic capacity and blood flow analysis assessed by single-photon-emission computed tomography (SPECT) nuclear imaging technology. SPECT analysis shows evidence that subjects treated with ALD-201 had improved blood flow with less ischemia in the heart at month six. Results show a statistically significant mean reduction in ischemia of 4.0% compared to a mean increase in ischemia of 3.7% in the placebo group (p=0.045). In the ALD-201 group, the mean amount of ischemia at six months was 2.6% versus 8.0% in the placebo group (p=0.012). MaxVO_2, a measure of aerobic capacity (the body's ability to take up oxygen during exercise), was greater in the ALD-201 group than in the placebo group over 6 months, though the change was not statistically significant. MaxVO_2 has been shown to be a predictive measure of mortality in patients with ischemic heart failure.

	ALD-201 (n=10)	Control (n=10)	
…Change In Ischemia (SPECT)	-4.0%	+3.7%	*p=0.045*
…Mean Ischemia at Six Months	+2.6%	+8.0%	*p=0.012*
…Improvement in MaxVO_2	+14.2%	+3.5%	*N/S*
…LVESV at Six Months	+7.8%	+0.2%	*N/S*

Based on the above data, management at Aldagen plans to progress into a phase 2 trial contingent on finding additional funding or a development partner. We expect that this phase 2 trial will assess the ability of ALD-201 to improve clinical and functional outcomes in patients with ischemic heart failure. We expect about 60 patients, randomized 1:1, with a primary endpoint of mortality and hospitalization for cardiac events. Secondary endpoints should include change in 6-minute walk distance, $MaxVO_2$, echocardiographic findings, including LVESV and other measures of muscular function, subjective measures of quality of life and changes in classification of heart failure (NYHA or CCS). A trial like this should cost between $3 and $5 million.

We see ALD-201 as having a fairly sizable market opportunity. For the 200-300k patients that have exhausted existing potential options for revascularization, ALD-201 could be a life-saver. The median hospital cost associated with heart transplantation is approximately $300,000. At a price of $25,000 per injection, with only 4% market share, ALD-201 has peak sales in the $200 to $300 million range.

ALD-301 – Critical Limb Ischemia



ALD-301 is a formulation of ALDH^{br} Cells designed to treat critical limb ischemia (CLI). CLI is a condition characterized by significant impairment of blood flow to the legs and feet caused by an obstruction of the arteries. Patients with severe cases of critical limb ischemia may experience persistent pain in their lower extremities and may also suffer from severe tissue damage in the affected area. It is the most advanced form of peripheral arterial disease (PAD), and can be associated with risk factors such as diabetes, high blood pressure, dyslipidemia, angina, and obesity. CLI affects approximately 1 million people in the U.S. each year – roughly 2% of the population over the age of 50. Over 25% of patients with PAD will eventually development CLI. CLI leads to an average of 160,000 major limb amputations each year. Mortality rate is high, 20% after 6-months after initial diagnosis and 25% after 12-months. Nearly 30% of all patients who undergo a major limb amputation will require another amputation at some point in the future. The mortality rate post-amputation remains high, at roughly 25%.

In late 2008, Aldagen initiated a phase 1/2 study with ALD-301 in patients with advanced CLI. In the trial, 21 patients were randomized to receive ten injections of ALD-301 (n=11) or unsorted bone marrow (n=10), and were followed for a total of 24 weeks, with efficacy assessment at 12 weeks post injection.

Patients enrolled were Rutherford 4 or 5 classification with no revascularization options. The primary endpoint was safety. Both ALD-301 and unsorted bone marrow cells were well-tolerated, with no serious adverse events associated with either option. The independent data safety monitoring board for the trial determined that the safety results supported further study of ALD-301 in CLI.

- Six of the 21 patients in the trial, including 4 of the 11 patients in the ALD-301 treatment group and 2 of the 10 patients in the unsorted bone marrow treatment group, experienced serious adverse events, such as hypotension, heart attack, angina, ischemic stroke, worsening critical limb ischemia, shortness of breath and worsening of leg ulcers. In each case, the investigators determined the serious adverse events to be related to the underlying disease and not to the receipt of either ALD-301 or the unsorted bone marrow cells.

- Over the course of the trial, one patient in the ALD-301 treatment group and one patient in the unsorted bone marrow treatment group required amputation of the treated leg, and the patient in the ALD-301 treatment group whose leg was amputated died approximately 50 days following the amputation, which was not considered by the investigators to be related to the therapy.

Efficacy was assessed at twelve weeks. The results were encouraging with respect to subjective classification on the Rutherford scale and quality of life measures, as well as some objective measures of clinical outcomes.

- The mean Rutherford category of the patients in the ALD-301 treatment group improved from 4.1 at baseline to 3.5 at 12 weeks. Four of the 11 patients in the ALD-301 treatment group experienced an improvement in Rutherford category to the degree that they were no longer classified as having CLI. None of the 11 patients in the ALD-301 treatment group experienced any worsening in Rutherford category. This compares favorably to the unsorted bone marrow group, where two of the 10 patients saw worsening in their Rutherford category.

- At week 24 following injection, 10 of the 11 ALD-301 patients were alive and amputation-free. Rest pain, as evaluated by VAS, decreased in the ALD-301 treatment group at 12 weeks compare to baseline. Quality of life, as measured by VascuQoL, increased in the ALD-301 group at 12 weeks compared to baseline.

- The mean ABI of the patients in the ALD-301 treatment group increased from 0.22 at baseline to 0.36 at 12 weeks. None of the 11 patients in the ALD-301 treatment group experienced a decline in ABI. The ankle-brachial index (ABI) is a widely used and reliable means for diagnosing PAD. An improvement in ABI of 0.1 is generally viewed as clinically meaningful. We note, however, that there was a similar increase in ABI for the unsorted bone marrow group.

- The mean $TcPO_2$ (transcutaneous oxygen) measure of the patients in the ALD-301 treatment group improved +9.5 mmHg at 12 weeks. This compared favorably to the +0.7 mmHg change in the unsorted bone marrow group. Mean $TcPO_2$ measure after 12 weeks in the ALD-301 group was 40.0 mmHg. Generally, a measure above 30.0 mmHg corresponds to an improved healing of skin ulcers.

An abstract of this phase 1/2 data was presented at the 2009 American Heart Association (AHA) meeting (Abstract#4934), later published in Catheterization and Cardiovascular Interventions, 2011,78:7:1060-67.

The next step for management would be a larger phase 2 study (~150 patients) comparing ALD-301 to a placebo, with clinical validated outcomes in CLI – most likely amputation-free survival at 12 months (AFS-12). This trial will be conducted in Rutherford 4-5 patients with "no option" for revascularization. We expect that, much like ALD-201, Cytomedix will seek additional funding or a commercialization partner before they proceed with additional studies on ALD-301 in CLI.

There are no FDA-approved drugs for the treatment of CLI. The predominant treatment options are surgical procedures to restore blood flow, or revascularization, such as implanting a new blood vessel to bypass the obstruction, or endovascular approaches, such as angioplasty. We estimate that 25% of all CLI patients have no option for revascularization. According to the U.S. Department of Health and Human Services, the median hospital cost associated with a leg amputation is approximately $50,000. With an annual treatment population of roughly 100,000 patients, with only 5% market share and a cost of $30,000 per treatment, ALD-301 has peak sales potential of $200 million.

We note that a competitor, Aastrom Biosciences, is currently conducting a phase 3 trial in no option CLI patients called REVIVE in approximately 600 patients. The trial has been given a special protocol assessment (SPA) and the treatment option, Aastrom's ixmyelocel-T, has been designated "Fast Track" status by the U.S. FDA.

ALD-401 – Ischemic Stroke



ALD-401 is a formulation of $ALDH^{br}$ Cells designed to treat ischemic stroke. Stroke is characterized by the rapidly developing loss of brain function due to a significant diminution in the blood supply to the brain. Strokes are typically classified into two major categories, ischemic and hemorrhagic. Ischemic strokes result from an inadequate supply of blood and oxygen to the brain due to blockage of an artery, such as by a blood clot, while hemorrhagic strokes result from rupture of a blood vessel or an abnormal vascular structure. The American Heart Association estimates that approximately 800,000 patients in the U.S. each year suffer a stroke; approximately 87% are ischemic.

Patients suffering an ischemic stroke can receive a tissue plasminogen activator (tPA). It is currently the only FDA-approved acute treatment for ischemic stroke. The drug is administered intravenously to break up clots and restore blood flow to the brain.

However, tPA is only approved for use within 3 hours of the onset of symptoms, and many patients who suffer an ischemic stroke are unable to reach a hospital for diagnosis and treatment within this period. The use of tPA can also lead to bleeding in the brain. There are no currently approved therapies for treatment of ischemic stroke after this three-hour period, which we refer to as post-acute treatment.

…Preclinical Data…

Aldagen has completed preclinical studies with ALDH^{br} Cells in collaboration with academic researchers at Duke University Medical Center. In this study, the middle cerebral artery in mice was temporarily blocked in order to induce a stroke. One group of mice was treated 14 days later by injecting ALDH^{br} Cells sorted from human bone marrow into their carotid arteries, while a second group was untreated. In this study, imaging showed that ALDH^{br} Cells migrated to the area of the tissue damage. And, at four weeks after the injection (six weeks after the stroke) neuromuscular coordination and motor abilities of the mice treated with ALDH^{br} Cells improved by 41% compared to an improvement of only 11% in the untreated group ($p<0.05$).

Data further show that brain volumes of the mice treated with ALDH^{br} Cells experienced a statistically significant slowing of decreased brain volume following the stroke when compared to the untreated mice ($p<0.05$). Magnetic resonance spectroscopy of biomarkers to measure stroke-induced decrease in cell viability showed that mice receiving treatment with ALDH^{br} Cells had a statistically significant reversal of stroke-induced decline in cell viability in the brain hemisphere opposite the stroke when compared to the untreated group ($p<0.05$).

In another study conducted in collaboration with the University of California at Davis, stroke was similarly induced in mice. Two weeks after the stroke, one group of mice was treated by injecting ALDH^{br} Cells into the carotid artery and another group was injected with a neutral delivery vehicle. The researchers used laser Doppler imaging to compare perfusion of the brains in the mice that received ALDH^{br} Cells with the brains of mice who received only the delivery vehicle. Brain perfusion was seriously impaired in both groups of mice two weeks after stroke, before the mice were treated. Four weeks after the treatment (six weeks after the stroke) the brains of the mice that received the delivery vehicle remained impaired, but perfusion in mice that received ALDH^{br} Cells had returned to normal levels. This is suggestive of increase in brain perfusion and potential angiogenic activity of ALDH^{br} Cells that could lead to restoring brain volume, brain cell viability and behavioral function following a stroke.

…Currently in Phase 2…

Aldagen is currently conducting a phase 2 study with ALD-401 in post-acute ischemic stroke called RECOVER-Stroke. It is a double-blind, placebo-controlled design, with a goal of enrolling 100 patients in a 60/40 randomization. ALD-401 will be administered to the patient via a single injection directly into the carotid artery approximately two weeks (13 to 19 days) following the stroke. The primary objective is to evaluate the safety of ALD-401 evaluated by the occurrence of adverse events in the two groups, as well as post-procedural changes in the diffusion-weighted MRI scan of the brain. Efficacy will be evaluated by change from baseline in the modified Rankin Scale (mRS) three months and changes from baseline in the NIH stroke scale and Barthel Index at three and six months.

As of late March 2012, eight patients have been enrolled in RECOVER-stroke. Management expects the next two patients to enroll shortly. Three centers are active. After the first 10 patients have cleared sequential DSMB review, the trial should open to an additional 12+ centers. RECOVER-stroke is enrolling only patients with unilateral ischemic strokes with an NIH stroke scale score between 7 and 22 prior to treatment.

As noted above, Aldagen shareholders can earn a 1.015 million share milestone for enrollment of the first 60 patients with DSMB clearance and a 3.046 million share milestone for completion of enrollment on or before May 31, 2013. Positive data from the phase 2 trial that results in progression towards a phase 3 program (successful end-of-phase 2 meeting with the U.S. FDA) can earn Aldagen shareholders another 16.248 million shares.

We are relatively confident that the safety endpoint after the first 60 patients enrolled will be met. Data published in the Annals of Neurology,2005;57-6:874-882, concludes that autologous mesenchymal stem cells can be safely administered without inducing serious adverse events, and may improve functional recovery in stroke patients.

…A High Risk / High Reward Program…

Stroke has been a minefield for drug development over the past decade. Small molecules and biologics tested in late-stage trials for acute ischemic stroke – eliprodil, selfotel, aptiganel, enlimomab, LeukArrest, nimodipine, fosphenytoin, maxipost, tirilazad, citocline, disutenton, diazepam, repinotan, nalmefene, and gangloside-GM1 to name a few – have all failed for one reason or another.

One thing to note about all the above failures – they are all one molecule going after one target. Cell therapy has the potential to use multiple mechanisms of action with multiple pathways for success. The most similar path to Aldagen's ALD-401 would be neural stem cells or neurotrophic factors.

- Neurotrophic Factors are a group of proteins involved in cell proliferation, migration, and differentiation. Preclinical studies demonstrate that neurotrophic factors such as nerve growth factor, BDNF, ciliary neurotrophic factor, glial-derived neurotrophic factor, vascular endothelial growth factor, and insulin-like growth factor (IGF)-1 can reduce infarct size in animal models. Phase 1 studies with basic fibroblast growth factor (bFGF) were encouraging, but all programs have been halted prior to phase 3 due to a lack of efficacy seen in mid-stage clinical trials.

- Neural Stem Cells, mainly found in the developing brain, are able to differentiate and regenerate in response to both internal and external stimuli. Research suggests that neural stem cells may be able to regenerate and restore loss of brain function in injuries such as stroke. This has been confirmed by numerous preclinical trials. A similar belief exists for bone marrow stromal cells, which have been shown to develop into neuroectodermal cells including neurons. Companies such as Neuralstem, San-Bio, and ReNeuron are pioneering this field. However, the clinical data remains early-stage.

The other aspect of RECOVER that is different from the above failed programs is the timing of the dose. ALD-401 will be dosed 13 to 19 days after the stroke. In most stroke trials, there is a rush to deliver within that three to six hour window. The only approved medication, tPA, must be dosed within three hours of the event. This has lead most companies to believe the window for an effective product is inside three hours. However, new evidence of stroke research shows that inflammation in the brain persists for two weeks after a stroke. There is also significant variability in baseline around the first few days after a stroke (with respect to mRS and NIH score) as the brain recovers. By allowing the inflammation to subside and the patient to stabilize, Aldagen believes dosing 13 to 19 days after the stroke gives ALD-401 a better chance to succeed.

We view the ALD-401 phase 2 program as different from many of the above failures. It's a novel approach, but the preclinical data looks encouraging. Work out of San-Bio, Neuralstem, and ReNeuron seems to confirm the theory behind the mechanism of action and the trial design. RECOVER is high risk, but given all the above failures and the wide-open market opportunity, it's all high reward.

Management estimates the annual patient population eligible for treatment with ALD-401 is between 176,000 and 265,000 patients (commissioned study by Trinity Partners). Trinity also estimates that the annual nursing home and in-home costs of the post-acute treatment of an ischemic stroke patient is approximately $30,000. The American Heart Association estimates the mean lifetime cost of ischemic stroke in the U.S. to be approximately $140,000. At an estimated price of $20,000 per ALD-401 treatment, with only 5% market share, ALD-401 has peak sales between $200 and $250 million.

We estimate the direct cost of the ongoing phase 2 RECOVER-stroke trial with ALD-401 is roughly $6 to $8 million. We are expecting enrollment to complete around the summer of 2013. We expect data about three to four month later, or late third quarter early fourth quarter 2013. If positive, we expect that management will be in position to meet with the U.S. FDA for the end-of-phase 2 meeting late 2013. A positive outcome from the phase 2 program forms the basis for a pivotal registration program to start in 2014. We expect management to quickly seek a development and commercialization partner for ALD-401 if the data are positive.

Our Thoughts On The Merger

We were admittedly surprised to see Cytomedix acquire a high risk drug development company like Aldagen. The core business with Angel is solid, and we believe that AutoloGel is on the verge of a major upward trajectory driven by Coverage with Evidence Development and a commercialization partnership with a major pharmaceutical company. That being said, the $4.5 million in exclusivity payments from the undisclosed pharma partner and the improving share price that allowed management to place $5 million in stock and exercise another $3 million in warrants all helped finance this potential significant leap forward for Cytomedix. Management believes they now have a strong foothold in the three pillars of regenerative medicine – Scaffolds, Signals, and Cells.

Plus, the deal actually isn't a major leap for Cytomedix. It is the same division of the FDA that regulates all three areas of the business and the potential synergies in drug delivery and manufacturing make sense to us. However, the phase 2 RECOVER program is the key driver near-term. We see the outcome as high risk / high reward. Programs with ischemic heart failure and critical limb ischemia offer future upside, and work done in this area by Cytori, Aastrom, Pluristem, Athersys, Osiris, et al. seems to validate the hypothesis. Aldagen's novel approach with highly viable, unaltered, autologous stem cells and little lead-time seems to give the company an advantage over many of the aforementioned players.

RECOMMENDATION

We have updated our financial model to include integration of Aldagen. We've add roughly $6 million in operating expenses for 2012 and $7 million for 2013. We've added some very minor revenues from AldeFluor and AldeCount. We have increased the share count by approximately 10 million shares immediately to account for the $5 million (4.2 million shares) private placement to existing Aldagen shareholders and the $3 million (5.7 million shares) warrant exercising from in-the-money Cytomedix holders. We expect a favorable shareholder vote on increasing the share count in the second quarter 2012, which will automatically convert the 135,398 Series-E preferred shares into 13.5 million shares of common stock. We expect that Cytomedix will exit 2012 with a basic share count of 88 to 90 million (depending on warrant exercises), with another 20+ million in future shares issuable upon Aldagen milestone and another near 15 million in warrants, options, and convertible debt. It is conceivable to see nearly 127 million shares outstanding by the end of 2013 with full dilution.

Basic Common Outstanding	**74.6 Million**
Series E (Automatic) Converts	**+13.5 Million**
Warrants (Ave. @ $0.88/share)	**+7.9 Million**
Options (Ave. @ $1.27/share)	**+8.2 Million**
Convertible Debt (Ave. @ $0.80/share)	**+2.2 Million**
Potential Milestones to Aldagen	**+20.3 Million**
Potential Fully Diluted Share Count	**126.7 Million**

Aldagen has twice canceled a planned initial public offering (IPO) due to poor market conditions, first in 2008 and most recently in April 2011. In April 2011, bankers were tossing around a firm value of around $80 million. We think this looks fair given the pipeline and comps with similar companies like Athersys, Aastrom, Neuralstem, Osiris, and Pluristem. As noted above, we see ALD-201 for ischemic heart failure having peak sales in the $200 to $300 million range. ALD-301 for critical limb ischemia (CLI) has peak sales in the $200 million range. ALD-401 for ischemic stroke has peak sales in the $200 to $250 million range.

Candidate & Indication	Peak Sales	Prob. Of Success	Discounted Value	Royalty On Sales	Adjusted Value	Valuation Multiple	NPV of Candidate
ALD-201 (heart failure)	$200 to $300 M	25%	$62.5 Million	Assume ~ 20%	$12.5 Million	2x Royalty	$25 Million
ALD-301 (PAD / CLI)	$200M	30%	$60 Million	Assume ~ 20%	$12 Million	2x Royalty	$24 Million
ALD-401 (ischemic stroke)	$200 to $250 M	25%	$56 Million	Assume ~ 20%	$11 Million	2x Royalty	$22 Million
ALDH^{br} Cells							$10 Million
						Total Firm Value	$81 Million

We see Aldagen's pipeline worth around $81 million. Adding $81 million to the previous $165 million firm value for Cytomedix brings us to $246 million in total value for the combined company. We believe that Cytomedix still needs an estimated $10 to $15 million in cash to reach breakeven operations, notwithstanding a potential U.S. deal for AutoloGel in June 2012. Therefore, a target value of around $230 million seems fair.

Based on the current basic share count of 88 million (including the 13.5 million Aldagen acquisition) of brings us to a target price of $2.60 per share. On a fully-diluted basis, which includes 20+ million shares for all Aldagen milestone associated with RECOVER and 15+ million warrants, options and convertible debt, brings us to roughly 127 million outstanding, or $1.80 per share. However, we note that if Cytomedix pays all of the 20+ million shares to Aldagen for a successful phase 2 RECOVER trial, ALD-401 will be worth far greater than $22 million in NPV. A successful phase 2 trial in post-acute ischemic stroke could quadruple the value we've assigned to ALD-401, and even spill-over to increase the value of ALD-201 and ALD-301, as well as the ALDH^{br} Cell platform. Positive data from RECOVER adjusts our fair-value target to approximately $315 million. And as noted above, a deal with a major pharmaceutical company for AutoloGel, assuming a modest upfront payment and profit-sharing / royalties on sales, adds another $40 to $50 million in value. Therefore, our target is $3.00 per share.

PROJECTED FINANCIALS

Cytomedix, Inc.
Income Statement

	2010 A	Q1 A	Q2 A	Q3 A	Q4 A	2011 A	Q1 E	Q2 E	Q3 E	Q4 E	2012 E	2013 E	2014 E	2015 E
AutoloGel	$0.37	$0.09	$0.11	$0.10	$0.09	$0.39	$0.10	$0.11	$0.20	$0.45	$0.86	$4.50	$15.50	$32.00
YOY Growth	61.8%	37.5%	15.8%	-21.4%	9.3%	5.2%	14.3%	0.0%	102.0%	405.6%	123.4%	423.3%	244.4%	106.5%
Angel System	$3.42	$1.28	$1.28	$1.43	$1.52	$5.51	$1.60	$1.65	$1.75	$1.85	$6.85	$8.45	$10.20	$12.24
YOY Growth	N/A	16.4%	22.1%	22.9%	25.6%	61.2%	25.0%	28.5%	22.4%	21.7%	24.2%	23.4%	20.7%	20.0%
Aldagen 3rd Party	*$0*	*$0*	$0	$0	$0	*$0*	$0.10	$0.10	$0.10	$0.10	$0.40	$0.50	$0.50	$0.50
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	25.0%	0.0%	0.0%
Med Product Sales	**$3.79**	**$1.37**	**$1.39**	**$1.53**	**$1.61**	**$5.90**	**$1.80**	**$1.86**	**$2.05**	**$2.40**	**$8.11**	**$13.45**	**$26.20**	**$44.74**
YOY Growth	1574.5%	2058.7%	21.5%	18.5%	24.7%	55.8%	31.8%	33.4%	34.1%	49.1%	37.4%	65.8%	94.8%	70.8%
Drug Pipeline	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Royalties & Collabs	**$0.12**	**$0**	**$0**	**$0**	**$1.3**	**$1.3**	**$2.0**	**$1.2**	**$0**	**$0**	**$3.2**	**$0**	**$0**	**$0**
YOY Growth	-100.0%	-	-	-	-	992.9%	-	-	-	-	-	-	-	-
Total Revenues	**$3.91**	**$1.37**	**$1.39**	**$1.53**	**$2.96**	**$7.25**	**$3.80**	**$3.01**	**$2.05**	**$2.40**	**$11.26**	**$13.45**	**$26.20**	**$44.74**
YOY Growth	89.3%	664.0%	21.5%	18.1%	128.9%	85.3%	178.3%	116.2%	33.8%	-18.8%	55.4%	19.4%	94.8%	70.8%
Cost of Sales	$1.80	$0.65	$0.64	$0.72	$0.73	$2.73	$0.81	$0.84	$0.92	$1.08	$2.76	$4.04	$7.07	$12.08
Product Gross Margin	52.5%	52.7%	54.2%	53.1%	54.9%	53.8%	55.0%	55.0%	55.0%	55.0%	66.0%	70.0%	73.0%	73.0%
R&D	$0.42	$0.06	$0.04	$0.00	($0.01)	$0.10	$0.72	$0.93	$1.24	$1.36	$4.25	$4.50	$3.80	$4.00
% R&D	10.6%	4.4%	3.0%	0.3%	-0.3%	1.4%	18.9%	30.8%	60.5%	56.7%	37.7%	33.5%	14.5%	8.9%
SG&A, Other Fees	$7.29	$2.14	$1.95	$1.84	$2.00	$7.94	$2.25	$2.45	$2.40	$2.35	$9.45	$9.50	$10.00	$10.50
% G&A	186.3%	156.9%	139.9%	120.3%	67.6%	109.5%	59.2%	81.3%	117.1%	97.9%	83.9%	70.6%	38.2%	23.5%
Operating Income	($5.40)	($1.48)	($1.24)	($1.03)	$0.24	($3.51)	$0.02	($1.20)	($2.51)	($2.39)	($5.19)	($4.59)	$5.33	$18.16
Operating Margin	-138.1%	-	-	-	-	-48.5%	-	-	-	-	-46.1%	-34.1%	20.3%	40.6%
Interest & Other Income	($1.40)	$0.08	$0.45	($1.17)	$0.66	$0.02	($0.05)	($0.05)	($0.05)	($0.05)	($0.20)	($0.15)	$0.20	$0.35
Pre-Tax Income	($6.80)	($1.41)	($0.79)	($2.20)	$0.90	($3.49)	($0.03)	($1.25)	($2.56)	($2.44)	($5.39)	($4.74)	$5.53	$18.51
Taxes	$0.01	$0	$0	$0	$0.0	$0.0	$0	$0	$0	$0	$0	$0	$0.6	$4.6
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	10.0%	25.0%
Preferred A, B, D, E	$2.22	$0.09	$0.09	$0.09	$0.09	$0.35	$0.09	$0.09	$0.09	$0.09	$0.36	$0.20	$0.10	$0.05
Net Income	($9.04)	($1.50)	($0.87)	($2.29)	$0.81	($3.86)	($0.12)	($1.34)	($2.65)	($2.53)	($5.75)	($4.94)	$4.87	$13.83
Net Margin	-231.1%	-	-	-	-	-53.2%	-	-	-	-	-51.1%	-36.7%	18.6%	30.9%
Reported EPS	**($0.23)**	**($0.03)**	**($0.02)**	**($0.04)**	**$0.01**	**($0.08)**	**($0.00)**	**($0.02)**	**($0.03)**	**($0.03)**	**($0.07)**	**($0.05)**	**$0.05**	**$0.12**
YOY Growth	150.7%	-	-	-	-	-67.4%	-	-	-	-	-10.5%	-23.8%	-183.3%	159.2%
FAS-123R Expense	$0.41	$0.10	$0.04	$0.07	$0.10	$0.31	$0.15	$0.12	$0.12	$0.15	$0.54	$0.60	$0.75	$0.75
EPS Impact of FAS-123R	*($0.01)*	*($0.00)*	*($0.00)*	*($0.00)*	*($0.00)*	*($0.01)*	*($0.00)*	*($0.00)*	*($0.00)*	*($0.00)*	*($0.01)*	*($0.01)*	*($0.01)*	*($0.01)*
Weighted Ave. Shares Out	38.7	46.1	50.6	52.3	61.6	50.7	70.5	88.1	89.0	90.0	84.4	95.0	105.0	115.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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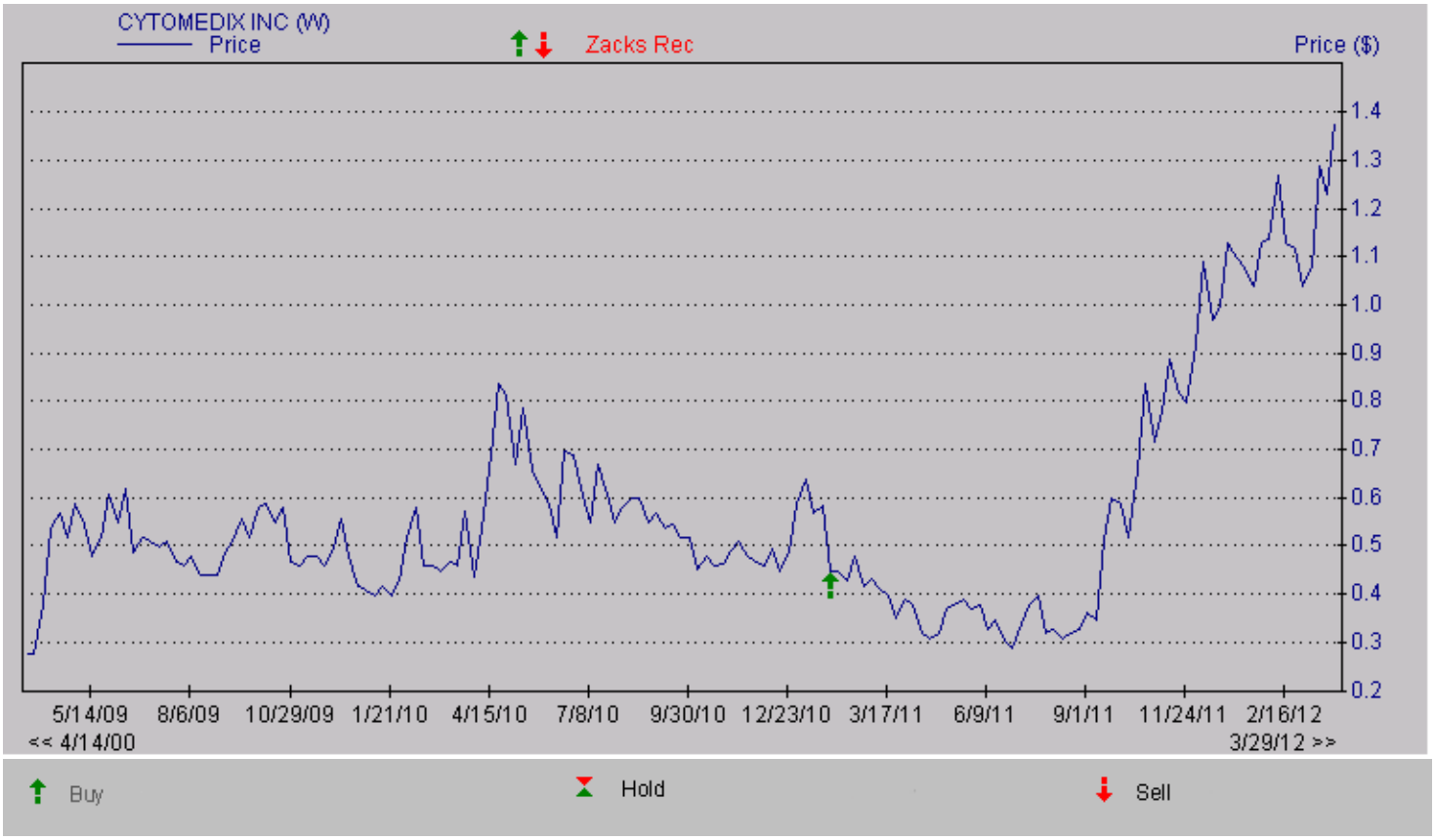

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