



INSTITUTIONAL RESEARCH

Healthcare & Biotechnology

INITIATION REPORT

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February 26, 2013

Arrowhead Research (Nasdaq/ARWR)

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BUY Homing in on Clinical Success

Arrowhead Research is a clinical stage targeted therapeutics company

Investment Highlights

1) Arrowhead has advanced its major internal product candidate, **Adipotide for Obesity, into the clinic**. The Phase 1 trial, sponsored and led by MD Anderson, began dosing patients in July 2012 with interim results expected to be ready sometime later this year. Obesity and weight loss is a large and growing market, and independent valuation of Adipotide's novel method of action in mice has been very promising.

2) The Company has also advanced its next internal product candidate, **ARC-520 for Hepatitis B virus**, with IND filing planned for the near-term second calendar quarter of 2013. Arrowhead is also planning to hold an extensive webcast next month to provide details on clinical trial strategy and timelines, the HBV market opportunity, and the intended product profile of ARC-520. Just this morning, Arrowhead announced the publication of data demonstrating multi-log reductions in hepatitis B viral DNA and proteins lasting over 30 days after a single injection in animal models. Recent buy-out valuation for clinical-stage companies in the Hepatitis C market have been staggering (Inhibitex, Pharmasset), and HBV therapeutics could be the next big thing in biotech M&A.

3) Arrowhead has compiled an impressive stable of partners for its discovery and development programs, including both large pharma and small but well-funded biotech firms. The Company's comprehensive RNAi platform is built around targeted, modular and efficient delivery while Arrowhead's innovative Dynamic Polyconjugate (DPCs) siRNA delivery system offers potential improvements over popular antibody-drug conjugates (ADCs), including cheaper, faster avenues to the clinic. ADCs have attracted a number of high-profile, high-value partnerships in recent years, including Merck-Endocyte; Immunogen-Lilly/Novartis and Seattle Genetics-Takeda and others, and DPCs may lead the next generation of biotech partnerships.

Current Price \$2.30

Price Target \$4.00

Estimates	F2012A	F2013E	F2014E
Revenues(\$000s)	\$147	\$2,000	\$9,000
EPS	(\$1.90)	(\$1.01)	(\$0.59)

Stock Data	
52-Week Range	\$1.75-\$7.31
Shares Outstanding (mil.)	17.3
Market Capitalization (mil.)	\$39.8
Enterprise Value (mil.)	\$37.8
Debt to Capital (12/12)	11.5%
Book Value/Share (12/12)	\$0.44
Price/Book	5.2 x
Average Trading Volume (3-Month)	85,500
Insider Ownership	31.6%
Institutional Ownership	2.9%
Short interest	290,000
Dividend / Yield	\$0.00/0.0%



Price target and ratings changes over the past 3 yrs:
Initiated - February 26, 2013 - Buy - Price Target \$4.00

4) Finally, Arrowhead has recently bolstered its balance sheet with two equity offerings and a note receivable sale transaction, positioning the Company well to deliver on near-term development catalysts.

Conclusion

Arrowhead has recently started one therapeutic into human clinical trials (Adipotide for Obesity), is set to start a second therapeutic in human trials later this year (ARC-520 for HBV), has compiled a large and growing stable of high-quality, high-profile development partners (including large names such as Merck and Shire and newer up-and-coming companies such as Alnylam and Cerulean), has beefed up its management team with new Chief Medical Officer and Chief Business Officer, and improved its balance sheet over the past one to two quarters. Still, ARWR shares have underperformed their peers in the red-hot RNAi and drug conjugate spaces, perhaps due to the Company's small market capitalization and investor unfamiliarity with a recent flurry of acquisition activity. We feel that as the Company's internal and partnership development programs progress and more investors become aware of Arrowhead's valuable technology and new operating capabilities, the Company's shares will begin to perform more positively along the lines of other biotech stocks in related areas. Thus, we are initiating coverage on ARWR shares with a BUY rating and 12-18 month price target of \$4.00 per share, using a discounted cash flow analysis valuation method.

Company History/Capitalization

Arrowhead Research Corporation (Arrowhead or ARWR) was incorporated in South Dakota in 1989 and reincorporated in Delaware in 2000. Arrowhead owns 74% of Calando Pharmaceuticals, which developed the RONDEL delivery system. In October 2011, Arrowhead purchased an RNAi therapeutics business assembled by Roche (OTCQX/RHHBY/Not Rated) including a state-of-the art research facility in Madison, Wisconsin and in April 2012 Arrowhead acquired privately-held Alvos Therapeutics, which owned technology licenses from MD Anderson Cancer Center related to homing peptides. The Company also holds ownership positions in Leonardo Biosystems, a drug delivery company, Ablaris Therapeutics, a drug delivery company, Nanotope, Inc., a regenerative medicine company, and previously Unidym, a nanotechnology company which was sold in early 2011.

Arrowhead's principal offices are located in Pasadena, California and the Company also operates a research and development facility in Madison, Wisconsin.

Company Business

Arrowhead Research is a clinical stage targeted therapeutics company with development programs in cancer, obesity and hepatitis B. The Company has developed or obtained a group of platform technologies and capabilities based on the mechanism of gene silencing RNA interference, or RNAi, and is leveraging these technologies to develop targeted therapeutic products. More specifically, these therapeutic drugs actively home in to cell types of interest while sparing off-target tissues, or accomplish non-specific uptake. The Company's lead delivery technologies include:

Dynamic Polyconjugates (DPCs) - The Dynamic Polyconjugate (DPC) platform is a small RNA delivery system that can be targeted to address multiple organ systems and cell types. DPC is a modular system that may be optimized on a target-by-target basis and has been demonstrated to promote multi-log gene knockdown in rodents and non-human primates and induce efficient endosomal escape. DPC has been shown further to allow wide safety margins using a variety of Short interfering RNAs (siRNAs) molecules.

Homing Peptides – Arrowhead’s Homing Peptide platform is a proprietary library of short peptides (short chains of amino acid monomers) that have demonstrated rapid and specific internalization into a wide variety of cell types. This library is currently being mined for the potential development of peptide-drug conjugates, or PDCs, and companion diagnostics. The Company plans to develop targeting peptides for use with its RNA delivery platforms as well as with traditional small molecule of peptide-based rugs.

RONDEL - Arrowhead’s RONDEL platform is a small RNA delivery system that has demonstrated effective systemic siRNA delivery, RNAi-mediated mRNA and protein knockdown in human melanoma patients.

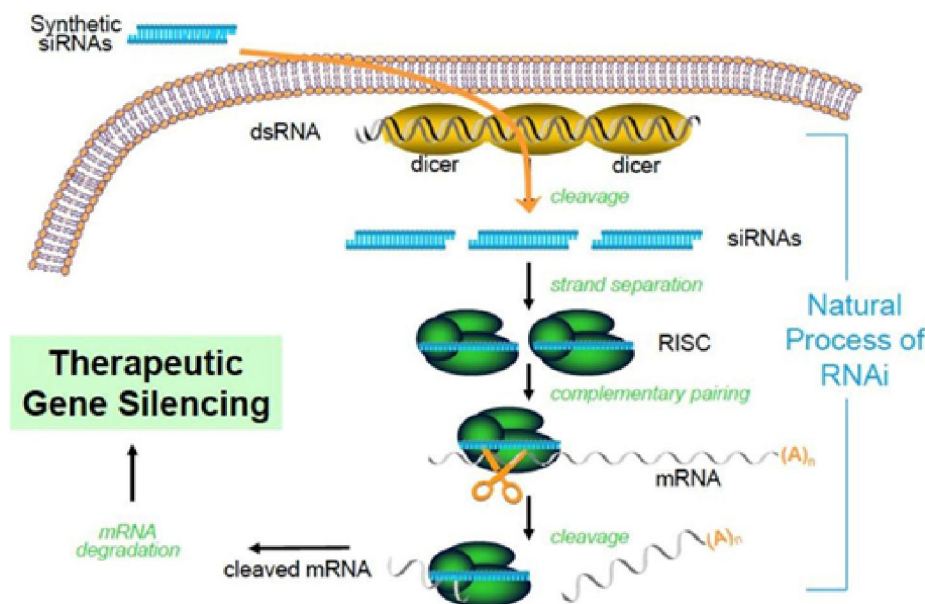
From these core technologies, the Company has developed several product pipeline candidates, including those developed both internally and with partners, as well as several primary strategic opportunities, which will be discussed in more detail below. First, however, we will go into further depth relating to the basic science behind the Company’s proprietary drug delivery and development platforms:

RNA Interference (RNAi) and the Benefits of siRNA Therapeutics

RNA interference (RNAi) is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Deemed to be one of the most important recent discoveries in life science with the potential to transform medicine, the discoverers of RNAi were awarded a Nobel Prize in 2006 for their work. Mediated by small interfering RNAs (siRNA), a class of ribonucleic acid (RNA) molecules 20-25 nucleotides in length, RNAi-based therapeutics can leverage this natural pathway of gene silencing to potentially target and shut down specific disease causing genes.

Small molecule and antibody drugs have proven effective at inhibiting certain cell surface, intracellular, and extracellular targets. However, certain drug targets, such as intranuclear genes and some proteins, have proven difficult to inhibit with traditional drug-based and biologic therapeutics. Developing effective drugs for these targets would have the potential to address large underserved markets for the treatment of many diseases. Using the ability to specifically silence any gene, siRNA therapeutics may be able to address previously unreachable targets, unlocking the large market potential of such targets or diseases. The chart below graphically depicts the natural process of RNAi interactions and potential effectiveness:

Diagram 1. Mechanism of RNA interference



The primary challenge to date in the development of siRNA therapeutics has been delivering the fragile, often immunogenic and otherwise rapidly cleared siRNA molecules into the cytoplasm of the cell, where RNAi activity occurs. This hurdle has prevented siRNA therapeutics from reaching full potential. Many companies have attempted to overcome the delivery challenge. Most early systems involved cholesterol conjugates or liposomes. However, development in humans has been limited due to toxicity and immunogenicity of these approaches when studied in clinical trials. Arrowhead has developed two modular delivery systems, Dynamic Polyconjugates and RONDEL that may be optimized on a target-by-target basis. Importantly, they also may be targeted to address a variety of tissues.

Dynamic Polyconjugates (DPCs) siRNA Delivery System

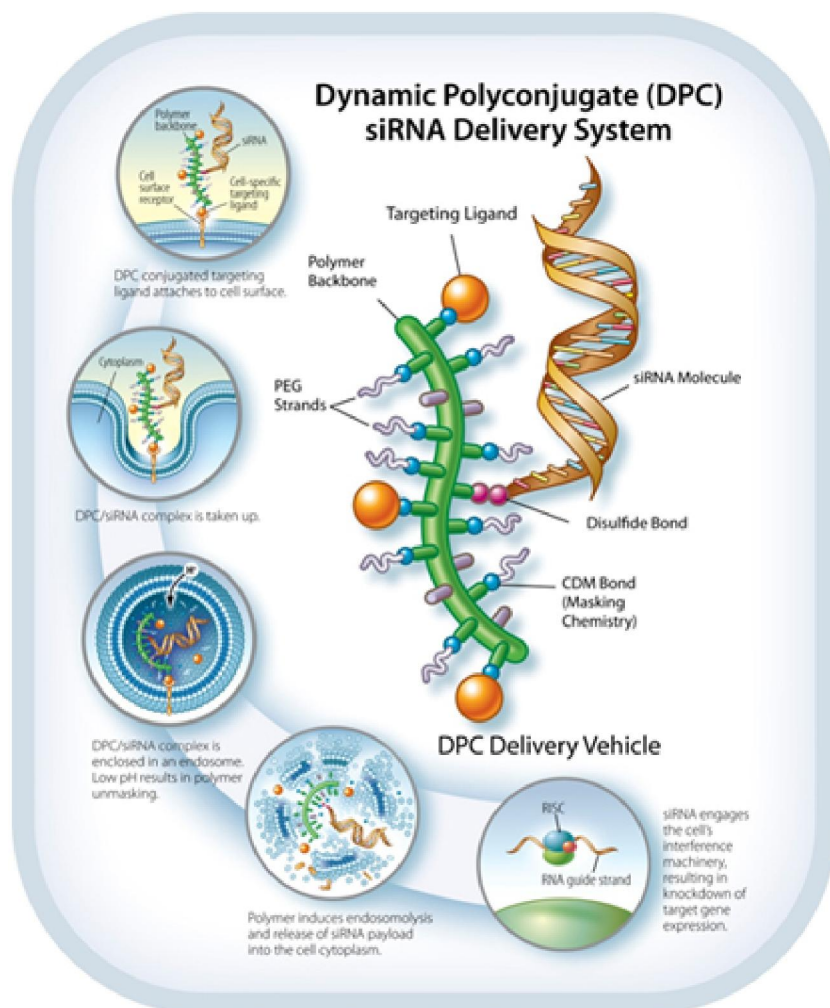
The DPC delivery system represents an innovative solution to the siRNA delivery problem, specifically designed to overcome barriers to systemic administration of siRNA. Developed in the Company's recently acquired Madison, Wisconsin laboratory, the inspiration for DPC technology came from the physical characteristics of viruses, nature's own nanoparticles, for nucleic acid delivery. Viruses are efficient at finding their target cells and delivering their nucleic acid payload to the proper cellular compartment. Key features of viruses are their small size, their overall negative surface charge, their specificity for particular cell types based on receptors unique to that cell, and their ability to disassemble and release their nucleic acid cargo to the proper cell compartment in response to cellular triggers. All of these features are incorporated into DPC technology.

DPCs are small nanoparticles, 5-20 nanometers (nm) in size, with an amphipathic polymer backbone. Arrowhead has a library of polymers that may be employed with the system, enabling optimization based on factors such as preferred mode of administration, pharmacokinetics, and target tissue. Shielding agents such as polyethylene glycol and targeting ligands are reversibly attached to the polymer backbone. In some constructs, the siRNA payload is attached to the DPC, while in other constructs the siRNA circulates attached to a different carrier. When attached, the DPC construct protects the siRNA payload while allowing the polymer to circulate in the blood without creating undue toxicity. The targeting ligand guides the nanoparticles to the cell of interest where, together with the siRNA, it is taken up into a membrane-enclosed cellular compartment known as an endosome. The particular polymer is selected for its ability to disrupt the endosomal membrane which releases the siRNA into the cytoplasm. There, it engages the cell's RNAi machinery, ultimately resulting in knockdown (or reduction) of target gene expression. This lytic (viral reproduction cycle) chemistry of the DPC polymeric backbone is modified, or "masked", using proprietary chemistry. Masking of the polymer's lytic chemistry accomplishes two interrelated objectives that are critical to in vivo siRNA delivery:

- Reduction of toxicity by controlling when the membrane lytic property of the polymer is activated; and
- Inhibition of non-specific interactions with blood components and non-targeted cell types.

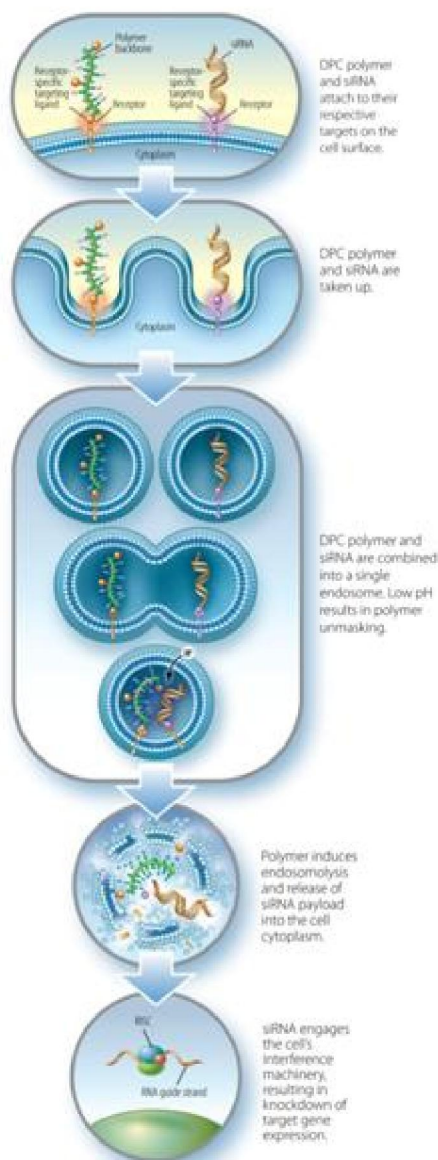
The diagram below depicts the interaction between the siRNA molecule and polymer backbone as well as the mechanism of action within the cell of the Company's DPC siRNA delivery system:

Diagram 2. DPC siRNA Delivery System



Arrowhead has developed multiple forms of the prototypical DPC delivery system. The Company's ARC-520 clinical candidate (described further below), for example, utilizes a formulation where the siRNA is conjugated to cholesterol and is not attached to the DPC. Pre-clinical studies have shown that co-injection of liver-targeted DPC polymer together with siRNA conjugated to a lipophilic moiety, such as cholesterol, results in a >500-fold increase in the potency when compared to the siRNA-cholesterol alone. This formulation retains the potent endosomal escape capabilities of Arrowhead's DPC platform, simplifies drug manufacturing, and creates new targeting opportunities. The diagram below portrays the Company's DPC co-injection strategy:

Diagram 3. DPC Co-injection Strategy

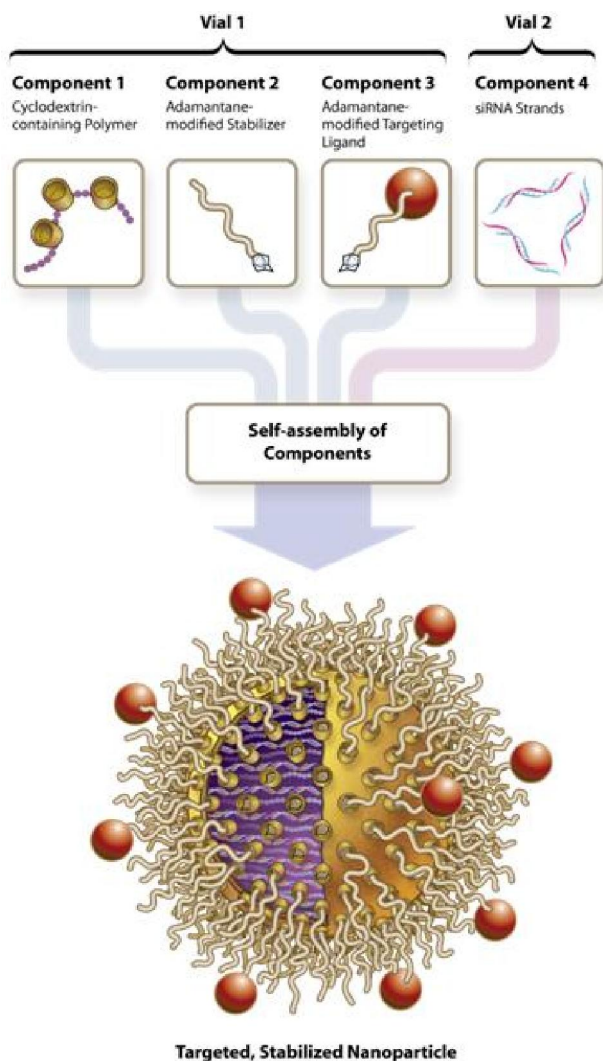


A DPC formulation for subcutaneous administration has also been developed using Arrowhead's latest proprietary polymer masking technology. Using DPCs to deliver siRNA, high-level target gene knockdown has been observed at low siRNA doses with limited toxicity in rodents and non-human primates. Arrowhead's studies have shown knockdown of 99% in monkeys after a single injection of 1 mg/kg, >90% at 0.5 mg/kg, and 80% in mice at 0.05 mg/kg, which represents greater knockdown at lower doses than reported results of other clinical candidates. Pharmacokinetic (PK) and biodistribution studies have indicated that this new masking technology is highly stable, allowing for maximum bioavailability and long circulation times. Arrowhead is developing this formulation for use in multiple therapeutic areas including oncology.

RONDEL Delivery System

Polymers form the foundation of Arrowhead's three-part RNAi/Oligonucleotide Nanoparticle Delivery (RONDEL) technology. The first component is the positively charged polymer that, when mixed with siRNA, binds to the negatively charged "backbone" of the siRNA. The polymer and siRNA self-assemble into nanoparticles less than 100 nm in diameter that are designed to protect the siRNA from nuclease degradation in serum. The cyclodextrin in the polymer enables the surface of the particles to be decorated by stabilizing agents and targeting ligands. These surface modifications are formed by proprietary methods involving cyclodextrins. The surface-modifying agents have terminal adamantane groups that form inclusion complexes with the cyclodextrin and contain polyethylene glycol (PEG) to endow the particles with properties that prevent aggregation, enhance stability and enable systemic administration. Targeting molecules can be covalently attached to the adamantane-PEG modifier, enabling the siRNA-containing particles to be targeted to tissues of interest. The diagram below portrays the four components (in two separate vials) which come together to assemble a targeted, stabilized nanoparticle within the Company's RONDEL delivery system:

Diagram 4. RONDEL Nanoparticle Components



Based on a novel polymeric sugar (linear cyclodextrin) molecule, RONDEL has been applied thus far to the delivery of two classes of therapeutics: siRNA and small molecule drugs. The polymer is combined with the drug molecule to form a drug-containing nanoparticle between 10 nanometers and 100 nanometers in size. Arrowhead believes that this particle size is important because drug molecules below 10 nanometers are quickly cleared from the body in the urine while nanoparticles larger than 100 nanometers are not always able to escape the tumor vasculature to reach tumor cells. Nanoparticles between 10 and 100 nanometers can lead to preferential accumulation in tumor tissue where the drug can take effect, leaving other tissues less affected. This drug delivery system has the added benefits of increasing solubility and allowing specific targeting of the nanoparticles.

The RONDEL delivery system offers the following advantages:

- **Generalized delivery system** — Binds to and self-assembles with the siRNA to form uniform colloidal-sized particles. Analysis has shown that these particles are spherical and between 10 nm and 100 nm in diameter;
- **Ease of siRNA sequence substitution** — Because RONDEL binds to the siRNA backbone, other siRNA sequences can be easily incorporated to form a new drug product;
- **Safety** — The RONDEL technology has been shown to have a positive safety profile in vitro testing with human cell cultures, and the fully formulated polymer/siRNA particles exhibit a significant therapeutic window of safety in animals, even when repeated doses (up to eight doses over a four week period) are used;
- **Effective targeted delivery** — The Company has demonstrated successful delivery of functional siRNA therapeutics to tumor cells and hepatocytes by systemic administration and confirmed sequence-specific gene inhibition; and
- **Human proof of concept** — CALAA-01, the first clinical candidate developed using the RONDEL system, has established several important “firsts” in human testing of a siRNA therapeutic — including first to show systemic siRNA delivery, first to show dose dependent accumulation in target cells and first to show RNAi mediated mRNA and protein knockdown.

CALAA-01 and RONDEL have been developed by Arrowhead’s majority-owned (74%) subsidiary, Calando Pharmaceuticals, Inc.

Homing Peptides Platform

Arrowhead’s homing peptides discovery platform is designed to identify targeting agents, such as peptides, that selectively accumulate in primary and metastatic tumors, associated vasculature, and as many as thirty healthy tissue types. Such targeting agents are of interest for drug development because they hold the promise of shepherding drugs into specific cells while sparing other cells. One of the key advantages of RNA delivery systems is their ability to be targeted. The Company is confident that due to its own proprietary targeting library, they can enhance the value of their existing RNAi programs and differentiate their capabilities from those of their competitors. In addition, the Company believes that they can apply the homing peptide sequences to non-RNA therapeutics and present attractive value to potential partners. The platform has the potential to allow Arrowhead to:

- Develop therapeutic agents that hunt down and destroy known tumors, as well as distant unidentified metastases;
- Convert cancer therapeutics that generally interact with most cells in the body to “smart” drugs that accumulate primarily at tumor sites and affect cancer cells preferentially, thereby improving the toxicity and side effects of currently used cancer drugs; and
- Selectively target non-cancer therapeutics to virtually any tissue type in the body where they can have the desired pharmacologic effect.

The homing peptide platform is potentially powerful in the specificity of the targeting sequences, the large number of unique sequences and their origin from human screening. In addition, because of the human-based identification process, there is lower risk that animal model data will not translate. Arrowhead’s proprietary library of 42,000 unique targeting sequences can be used with the Company’s own delivery platforms, as well as with small molecule drugs. This platform has achieved clinical proof of concept in targeting metastatic prostate cancer with the first sequence tested in humans.

Drs. Renata Pasqualini and Wadih Arap, who developed the Homing Peptide platform technology, operate a large laboratory at MD Anderson Cancer Center. They focus on discovering novel cell-surface receptors and validated receptors on tumor sites and identifying peptide sequences that will bind to those receptors. Importantly, their method identifies peptides that are rapidly internalized into cells. These peptide-receptor pairs hold the promise of shuttling therapeutic payloads preferentially and directly into those cells. The ability to target and deliver cytotoxins could address some of the problems with current cancer therapeutics by limiting side effects and increasing efficacy.

In order to discover these receptors and sequences that target them, Drs. Pasqualini and Arap used a technique called in vivo phage display. Over the past several years they have applied phage display screening to end-stage cancer patients with primary and metastatic tumors under rigorous ethical standards. To the Company’s knowledge, they are the only working group world-wide that is generating this type of human-derived data. Direct screening in human cancer patients has the potential to eliminate some of the uncertainty that has plagued current discovery methods with animal models. This strategy sought to map the human vasculature into “zip codes” and has discovered a large number of novel receptors that are expressed only on the cell surface of tumor sites and nowhere else. The library can be further increased by continuing to work with MD Anderson to screen additional patients.

Arrowhead is working to apply this technology to targeting their proprietary siRNA delivery vehicles. These two primary delivery platforms, DPCs and RONDEL, are highly attractive in part because they have been shown to be well tolerated, effective, capable of delivering RNAs to multiple organ systems, and they are targetable. The Homing Peptide library provides the Company’s targeted therapeutic program with a new source of flexibility. The library is also valuable in creating a new class of therapeutics, Peptide-Drug Conjugates, or PDCs. By linking the Homing Peptides to traditional small molecule drugs, a therapeutic that interacts with most cells in the body can potentially be transformed into one that interacts preferentially with the cell of choice. The Company believes that this transition from untargeted to targeted drugs is a paradigm shift for cancer therapeutics and that the Homing Peptide library puts Arrowhead at the forefront of this transformation. Arrowhead intends to build an internal pipeline as well as work with partners to apply proprietary targeting sequences to therapeutics owned by potential partners. In addition, this specific targeting ability could enable the development of safer and more effective generic drugs and the Company intends to work with partners to help make their proprietary drugs better. Given the large number of approved APIs for oncology and the thousands of Homing Peptide sequences that the Company owns, there are many potential combinations of targeting sequence and drug molecules.

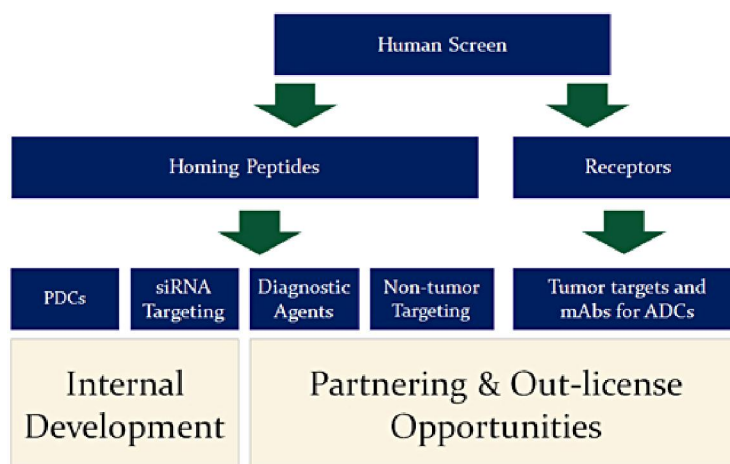
PDCs share the promise of the original class of guided therapeutics, antibody-drug conjugates or ADCs, in that they could increase efficacy and decrease toxicity relative to current standard of care oncology products. (Most notable examples are Mylotarg for acute myelogenous leukemia and Adcetris indicated for Hodgkin's lymphoma.) Benefits of PDCs as a class are as follows:

- They are potentially faster, cheaper, and simpler to make than ADCs, making them attractive development projects for biopharmaceutical companies;
- Their targets are expressed on a high percentage of multiple tumor types, giving them a larger potential commercial market than genetically targeted agents that are efficacious in only a small subset of patient populations; and
- The use of Homing Peptides that were discovered in human cancer patients as the targeting moieties for PDCs potentially increases clinical probability of success.

The Company believes that this unique mix of benefits will be attractive to potential partners in the biopharmaceutical industry. This technology has the potential to facilitate the rapid development of multiple new product candidates, each of which could meet a critical unmet medical need. In addition, screening in man has broad applicability in other therapeutic areas of interest to the biopharmaceutical industry.

The chart below provides a breakdown of the commercialization strategy and opportunities for Arrowhead through their Homing Peptides platform:

Diagram 5. Commercialization Opportunities for Homing Peptide Platform












Pipeline Overview

Arrowhead is focused on delivering drugs preferentially to their site of action while avoiding non-specific uptake in off-target tissues. The Company's platform technologies are being developed to enable new therapeutic modalities through targeted delivery and enhanced pharmacokinetics. In particular, Arrowhead's polymeric delivery systems, Dynamic Polyconjugates and RONDEL, have been formulated with small RNAs to develop drug candidates to address diseases such as cancer and Hepatitis B through the mechanism of RNA interference. The ability to deliver the fragile siRNA molecules that induce RNAi is the key enabler of this important new field of medicine. The Company's Homing Peptide platform is being used in a clinical obesity therapeutic study and in preclinical studies targeting cancer.

The Company's internal preclinical and clinical development programs are designed to create value directly through proprietary candidates. These programs also drive value to the technology platforms as proof of concept for the ability to develop innovative new therapies and enhance the effectiveness and safety of more traditional small molecule drugs. The diagram below outlines the Company's internal and partnered developmental pipeline delineated by platform technologies, including RNA interference, Homing Peptides, and Cycloset:

Diagram 6. Arrowhead Research Development Pipeline

	Product	Indication	Rx Mode	Partner	Pre-clin	Pre-IND	P1	P2
RNA Interference	CALAA-01	Oncology	siRNA	Internal				
	ARC-520	Hepatitis B	siRNA	Internal				
	Hif-2α	Renal Cell Carcinoma	siRNA	Internal				
	Undisclosed		siRNA	Alnylam				
Homing Peptides	Adipotide (Prohibitin TP-01)	Obesity / Metabolic Disorder	PDC	Internal				
		Oncology	PDC	Internal				
	Undisclosed		PDC	Shire HGT				
Cycloset	CRLX-101	NSC Lung Cancer	Small Molecule	Cerulean Pharma				
	Tubulin Inhibitor	Oncology	Small Molecule	Tube Pharma				

ARC-520 – Hepatitis B Virus Infection

In Arrowhead's comprehensive White Paper on Hepatitis B Virus and Potential RNAi Treatment dated March 7, 2012 the Company cites a recent estimate from the World Health Organization that 360 million people worldwide are chronically infected with the hepatitis B virus, of which 500,000 to 1 million die each year from HBV-related liver disease, which can include cirrhosis, decompensated cirrhosis, end-stage liver disease, and hepatocellular carcinoma. Furthermore, although chronic hepatitis B is often characterized as a disease that predominantly affects the developing world, current costs of treatment, diagnosis and prevention are significant in the largest world markets. For example, in the United States alone, there are 1.25 million individuals living with chronic hepatitis B with over 60,000 new cases diagnosed annually.

Chronic hepatitis B can be a dynamic and complex disease, as described in a 2009 publication from The European Association for the Study of Liver Disease (EASL) which divided the disease into five phases as outlined below:

- Immune Tolerant Phase – This first phase is more frequent and prolonged in perinatally-infected (pre-birth) patients or those infected in the early years of life. It is characterized by HBeAg (hepatitis B envelope antigen) positivity, high levels of HBV replication, normal or low levels of aminotransferases, and mild or no liver involvement. Patients in this stage are highly contagious.
- Immune Reactive Phase – This phase may occur after several years of immune tolerance and is more frequently observed in patients infected during adulthood. It is characterized by HBeAg positivity, a lower level of HBV replication, increased or fluctuating levels of aminotransferases, and a greater degree of liver involvement than in the Immune Tolerant phase.
- Inactive HBV Carrier State – This phase may follow seroconversion from HBeAg positive to anti-HBe antibody positive. It is characterized by very low or undetectable serum HBV DNA levels and normal aminotransferases. This state is associated with a favorable long-term outcome with a very low risk of cirrhosis or hepatocellular carcinoma in the majority of patients.
- HBeAg-negative Chronic Hepatitis B – This critical phase may follow HBeAg seroconversion during the immune reactive phase and represents a later stage in the natural history of chronic hepatitis B. It is characterized by periodic reactivation with a pattern of fluctuating levels of HBV DNA and aminotransferases and active hepatitis. Although patients in this phase are HBeAg negative, they harbor HBV variants with mutations in the precore and/or basal core promoter regions and so are unable to express or express only low levels of HBeAg. In contrast to patients who have truly seroconverted from HBeAg to anti-HBe antibodies and who have a good prognosis, these patients have active liver disease, with a high risk of progression to advanced hepatic fibrosis, cirrhosis and subsequent complications such as decompensated cirrhosis and hepatocellular carcinoma.
- Hepatitis B surface antigen (HBsAg)-negative Phase – In this final phase of HBV infection, low levels of HBV replication may still occur in the liver after loss of HBsAg. HBsAg loss is associated with improvement in outcome with a lowered risk of cirrhosis, decompensation and hepatocellular carcinoma. Immunosuppression can lead to reactivation in these patients.

Chronic HBV infection is defined by the presence of hepatitis B surface antigen (HBsAg) for more than 6 months. In the immune tolerant phase of chronic infection which can last for many years, an infected patient typically produces very high levels of viral DNA and viral antigens. However, the infection is not cytotoxic and the carrier may have no symptoms of illness. Over time, the ongoing production of viral antigens causes inflammation and necrosis, leading to elevation of liver enzymes such as alanine and aspartate transaminases, and later hepatitis, fibrosis, and liver cancer (HCC). If untreated, as many as 25% to 40% of chronic carriers develop cirrhosis or HCC. Antiviral therapy is prescribed when liver enzymes become elevated.

The current standard of care for treatment of chronic HBV infection is a daily oral dose of nucleotide/nucleoside analogs (NUCs) or a regimen of interferon injections 2 to 7 times weekly for approximately one year. NUCs are generally well tolerated, but patients may need lifetime treatment because viral replication often rebounds upon cessation of treatment. A number of NUCs are currently marketed in the US, including:

- Zefflix/Epivir-HBV (lamivudine) by GlaxoSmithKline (NYSE/GSK/Not Rated);
- Hespera (adefovir dipivoxil) and Viread (tenofovir) by Gilead Sciences (Nasdaq/GILD/NR);
- Baraclude (entecavir) from Bristol Myers-Squibb (NYSE/BMY/NR); and
- Tyzeka/Sebivo (telbivudine) by Novartis (NYSE/NVS/NR) and Idenix (Nasdaq/IDIX/NR)

Interferon therapeutics can result in a functional cure in up to 20% of some patient types, but treatment is often associated with significant side effects, including influenza-type symptoms (fatigue, myalgias, and fever), cytopenia, depression, anxiety, irritability and autoimmune disorders. The leading interferon-based therapeutics include both pegylated (pegINF) and non-pegylated forms. pegINF has a longer half-life than its non-pegylated

counterpart, allowing it to be dosed once, instead of three times weekly. Administration of both forms of interferon is accomplished via subcutaneous injection.

Arrowhead believes there is a need for a next generation HBV treatment with fewer side effects, that eliminates the need for interferon based treatment, has a finite treatment period and an attractive dosing regimen, and one that can be used at earlier stages of disease. The Company believes that a new therapeutic approach that can effectively treat or provide a functional cure (development of patient antibodies against HBsAg) has the potential to take significant market share and may expand the available market to include patients that are currently untreated. ARC-520 is Arrowhead's novel siRNA therapeutic intended for delivery to the active site of infection using the proprietary Dynamic Polyconjugate (DPC) technology. ARC-520 consists of two siRNA duplexes, each conjugated to a cholesterol derivative to enhance liver delivery and cellular uptake. ARC-520 has been designed to be co-administered with an active excipient, a masked, hepatocyte targeted polymeric amine. Once the siRNAs and the active excipient are taken up by the hepatocytes, the polymeric amines are unmasked in the endosome and disrupt the endosomal membrane, releasing the siRNA to the cytoplasm where it can engage the RNAi machinery of the cell.

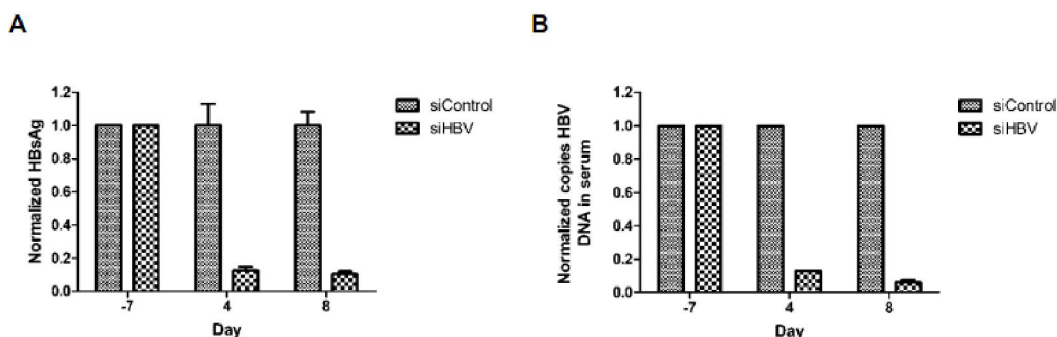
The siRNAs in ARC-520 are designed to target multiple components of HBV production including the pregenomic RNA that would be reverse transcribed to generate the viral DNA. The siRNAs in ARC-520 target the mRNAs that produce HBsAg proteins, the viral polymerase, the core protein that forms the capsid, and the HBeAg. A reduction of viral antigens is considered necessary to effective therapy because the presence of viral proteins is thought to be a major contributor to the persistence of liver disease secondary to HBV infection.

The company is currently conducting IND-enabling studies and is planning to enter a Phase I clinical study in Mid -2013.

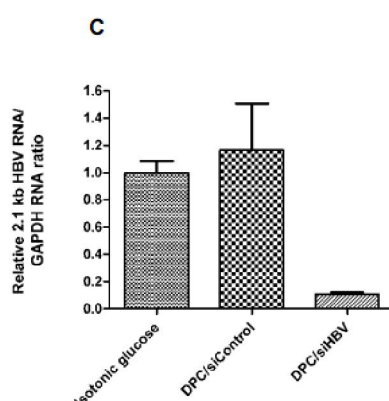
Results from preclinical studies from Arrowhead's HBV program have been presented at recent scientific conferences. Single-dose injections of hepatocyte-targeted anti-HBV siRNA DPCs in a replication-competent, transiently transgenic HBV mouse model resulted in a multi-log reduction of serum HBsAg and serum HBV DNA. Using a transgenic mouse model of chronic HBV infection, dramatic reductions in viral transcripts, viral replicative DNA intermediates, and intracellular HBV core antigen were observed in the liver after two weekly doses. In multi-dose studies in mice carrying a hepatocyte-specific reporter gene fused to HBV sequences, four biweekly injections of anti-HBV siRNA DPCs resulted in a multi-log reduction in gene expression over 2 months without changes in toxicity markers.

Efficacy data in mouse models of HBV infection show that ARC-520 is capable of reducing HBsAg by greater than 3 log (99.9%), HBV DNA by approximately 3 log, and HBeAg to the limit of detection. Pharmacologic effects persist for approximately one month after a single dose of ARC-520. Safety data in rodents and non-human primates indicate an acceptable safety margin.

To test the efficacy of Arrowhead's DPC technology for delivery of anti-HBV siRNAs, a nontransgenic mouse model of chronic HBV infection of the liver was established. These mice produce HBsAg and HBV viral particles that are secreted into the blood. The mice were then given a single injection of 1.5 mg/kg DPC with 0.2 mg/kg siRNA that targeted HBV. One week later, HBsAg levels in the serum were reduced by 90% (Chart A below) and the amount of HBV DNA in the blood was reduced by 94% (Chart B).



DPC containing siRNA targeting HBV were also shown to be highly effective against a transgenic mouse model of chronic HBV infection (Chart C below). Transgenic HBV1.3.32 mice were given a single injection of 2 mg/kg DPC with 0.5 mg/kg HBV siRNA. Four days later, the level of 2.1 kilobase messenger RNA that codes for HBsAg was knocked down by 89%.



In November 2012, Arrowhead created a clinical advisory board specifically focused on the Hepatitis B virus. The board is to be chaired by Dr. Robert Gish, who currently is Clinical Professor, Section Chief of Hepatology, at the University of California, San Diego and Medical Director for the Center of Excellence for Hepatobiliary Disease and Abdominal Transplantation (CHAT). Previously, Dr. Gish was the Co-Medical Director at the California Pacific Medical Center in San Francisco and became the Medical Director of the Liver Transplant Program in 1995. Dr. Gish has extensive experience in Hepatology-related clinical programs and will be responsible for recruiting additional members of the newly-established Hepatitis B clinical advisory board.

The company is currently conducting IND-enabling studies and is planning to enter a Phase I clinical study in calendar Q2/2013. Along these lines, Arrowhead initiated final IND-enabling GLP toxicology studies in December 2012, with the in-life portion of these studies expected to be completed later in calendar Q1/2013. Histology of these studies is expected to be completed in March and a final audited draft report is hoped to be made available in Q2/2013 to support the planned clinical timeline. Finally, Arrowhead continues to work on completing GMP manufacturing of the clinical supply and Company management expects this to be completed in Q2/2013.

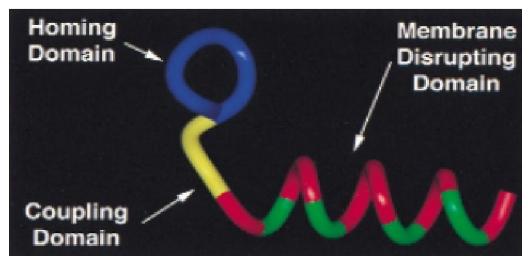
Furthermore, in a recent quarterly conference call, Arrowhead management stated that in March 2013 the Company plans to conduct a webcast describing in detail the development of ARC-520, HBV disease biology,

current standard of care, the HBV market opportunity, ARC-520's intended product profile, clinical trial strategy and timelines, as well as new data.

Adipotide (Formerly Prohibitin-TP01) – Obesity and Metabolic Disorders

Obesity is a global health threat and one of the leading causes of preventable deaths in the United States. Arrowhead's anti-obesity drug candidate, Adipotide, was designed to selectively disrupt the blood supply that supports unhealthy fat by the targeted induction of apoptosis (cell death) in the vasculature of adipose tissue. The Adipotide peptide consists of two functional domains. The homing domain targets a membrane associated protein, Prohibitin, on adipose vascular endothelial cells. The membrane disrupting domain causes apoptosis by disrupting mitochondrial membranes inside the cells. The diagram below depicts the method of action of Adipotide as it specifically targets membrane-associated Prohibitin on adipose vascular endothelial cells:

Diagram 7. Adipotide Method of Action

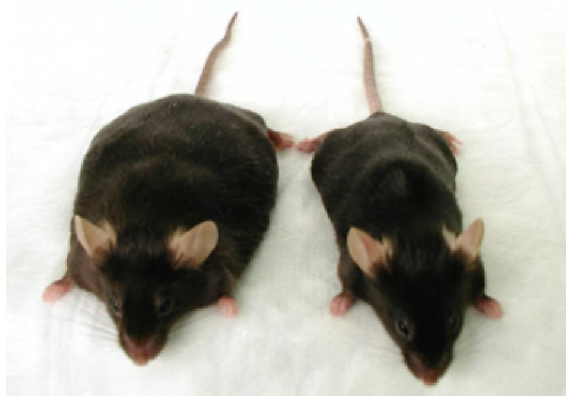


Adipotide is based on Arrowhead's Homing Peptide library developed at the MD Anderson Cancer Center. White adipose (fat) tissue is highly vascularized and both the expansion and maintenance of adipose tissue depend on a continued ability to build supporting vasculature. This peptide targeting library provides a map of the unique cell receptors on the vasculature that varies in different tissues. Targeting vasculature based on this variation allows for specific delivery of drug payloads to specific target cells, while avoiding collateral injury to other healthy/non-targeted cells. Using this technique, peptide sequences that target receptors specific to white adipose tissue were identified. Adipotide has been developed by the Company's majority-owned subsidiary, Ablaris Therapeutics, Inc. ("Ablaris"). Arrowhead owns 64% of the fully diluted shares of Ablaris.

In preclinical proof of concept studies, Adipotide was found to have the following therapeutic advantages:

- Loss of 30% of body weight in 4 weeks;
- Fat ablation and appetite suppression;
- Reduction in symptoms of diabetes; and
- Reversal of steatosis (fatty liver).

The illustration below portrays several of the mice from the preclinical study:

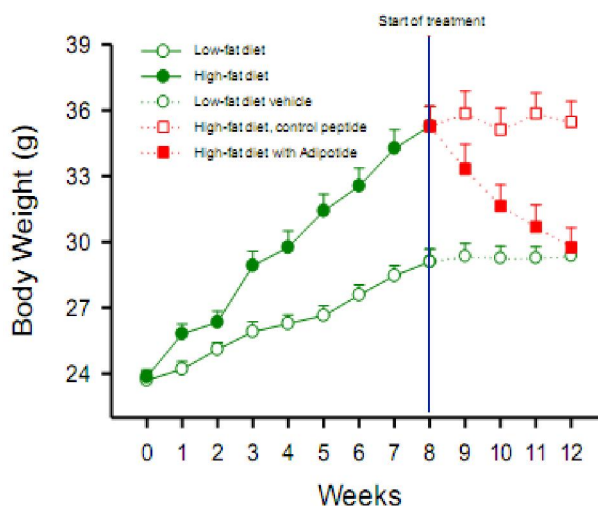


In an independent validation study led by Dr. Randy Seeley (Kim DH, Woods SC, Seeley RJ. "Peptide designed to elicit apoptosis in adipose tissue endothelium reduces food intake and body weight." *Diabetes* (2010) 59(4): 907-15.), Adipotide was found to have the following positive attributes:

- Adipotide reversed high fat diet-induced obesity in mice in 4 weeks;
- No effect on lean mice on low fat diet; and
- Most of weight loss was due to decreased food intake.

Dr. Seeley is the Director of the Cincinnati Diabetes and Obesity Center and Professor of Pathobiology and Molecular Medicine, University of Cincinnati. Dr. Seeley's expertise is in metabolism and obesity, with over 150 publications in the area, including several follow-on diabetes and obesity studies related to this area. The chart below depicts the results of the independent study led by Dr. Seeley:

Diagram 8. Independent Validation of Adipotide Measuring Body Weight versus Weeks of Treatment



In January 2012, the Company announced that its Investigational New Drug Application (IND) for Adipotide was accepted by the US FDA, and Arrowhead began enrolling patients in July 2012 as part of a Phase 1 clinical trial to test the safety of the compound in human patients. Arrowhead's collaborator, MD Anderson Cancer Center in Houston, plans to enroll up to 39 obese prostate cancer patients in the Phase 1 study and has agreed to

bear all direct costs of this trial. Up to five dose levels of the drug candidate will be tested in the trial. Three participants will be enrolled at each dose level, with the first group of participants receiving the lowest dose level by injection under the skin once per day for 28 days and each new group receiving a higher dose than the group before it, if no intolerable side effects are seen. This will continue until the highest tolerable dose is found or the study terminates.

CALAA-01 – Solid Tumors

CALAA-01 is an RNAi-based therapeutic that targets solid tumors. It employs the RONDEL RNAi delivery technology and completed a phase 1b clinical trial in 2012. CALAA-01 is a combination of RONDEL and a patented siRNA targeting the M2 subunit of ribonucleotide reductase, a clinically-validated cancer target. Ribonucleotide reductase catalyzes the conversion of ribonucleosides to deoxyribonucleosides and is necessary for DNA synthesis and replication; it is a critical component in the proliferation of cancer cells. The siRNA and CALAA-01 have demonstrated potent anti-proliferative activity across multiple types of cancer cells.

Interim clinical results were presented at the 2010 American Society of Clinical Oncology meeting (ASCO). Data from 15 patients accrued to 5 dose levels (3, 9, 18, 24, 30 mg/m²) showed that treatment-related adverse events were mostly mild to moderate with fatigue, fever/chills, allergic, or gastrointestinal-related adverse events most frequently observed. Importantly, no changes in coagulation, liver function tests, or kidney function were observed.

Analysis of tumor biopsies from three melanoma patients showed the presence of intracellular nanoparticles in amounts that correlated with dose. Additionally, a reduction was found in both the RRM2 messenger RNA and protein levels when compared to pre-dosing tissue. Furthermore, the presence of siRNA-mediated mRNA cleavage products was confirmed by 5'-RACE, demonstrating that siRNA-mediated mRNA cleavage occurred specifically at the site predicted for an RNAi mechanism. These results were published in March 2010 in the scientific journal *Nature*, citing these interim data from this Phase 1 trial as the first evidence of systemic delivery of siRNA, and the successful “silencing” of a widely recognized cancer gene via RNA interference in humans.

Enrollment in the Phase 1b clinical trial, conducted by the Company's Calando Pharmaceuticals subsidiary, was completed in August 2012. The trial was an open-label, dose-escalating study of the safety of intravenous CALAA-01 in adults with solid tumors refractory to stand-of-care therapies. Patients who satisfied the inclusion and exclusion criteria received two, 21-day cycles of CALAA-01. A cycle will consist of four infusions administered on days 1, 3, 8, and 10 followed by 11 days of rest. If safe, a second 21-day cycle was administered consisting of infusions on days 22, 24, 29, and 31 followed by 11 days of rest. Arrowhead is in the process of finalizing and analyzing the trial data for presentation at a future research meeting.

Cycloset and CRLX-101 (formerly IT-101)

CRLX-101 is an experimental, nanoparticle therapeutic that consists of the drug camptothecin (CPT) conjugated to a cyclodextrin polymer. CRLX-101 is based on the Cycloset delivery platform, a linear cyclodextrin polymer similar to the one used in the RONDEL system, which was developed by the Company's scientists as a delivery platform for small molecule drugs. Both CRLX-101 and Cycloset have been partnered with Cerulean Pharma, Inc., a Cambridge, Massachusetts-based biotechnology company, which has completed enrollment for a phase II clinical trial in non-small cell lung cancer.

In June 2009, Cerulean licensed rights to further research and commercialization of IT-101 (now known as "CRLX-101"), and the Cyclosert platform for all products except for nucleic acids, tubulysin, cytolysin and second generation epothilones from Arrowhead. In connection with the transaction, the Company assigned certain patents to Cerulean and Cerulean granted back to Arrowhead rights necessary to research and commercialize the excluded products. As such, the Company retains the rights to the RONDEL siRNA delivery platform, as well as CALAA-01. Arrowhead received an initial payment of \$2.4 million, and may receive development and sales milestones, and royalty payments if CRLX-101 or other products based on the Cyclosert platform are successfully developed. Should Cerulean sublicense CRLX-101 to a third party, the Company is entitled to receive a percentage of any sublicensing income at rates between 10% and 40%, depending on the stage of the drug's development at the time of sublicensing.

In addition to the already-completed phase 2 trial with CRLX-101 in non-small cell lung cancer, Cerulean Pharma currently has several additional ongoing phase 2 studies of CRLX-101, in small cell lung cancer, gastric cancer, ovarian cancer, and renal cell carcinoma. Arrowhead management believes that results from the 150-patient Phase II trial in non-small cell lung cancer is due to be reported by Cerulean this quarter, and also that Cerulean anticipates that another drug candidate will be created with the Cyclosert platform and the chemotherapeutic Docetaxel in early 2013. Arrowhead is also eligible for milestones payments on that candidate. Recently, Cerulean announced the completion of a \$13 million Series D round equity financing with existing and new venture funds and institutional investors.

Alnylam - Undisclosed siRNA Target

In January 2012, Arrowhead and Alnylam Pharmaceuticals (Nasdaq/ALNY/NR) formed a collaboration and joint licensing agreement related to Arrowhead's Dynamic Polyconjugate (DPC) delivery technology for an RNAi therapeutic product. Alnylam expects to deploy this technology for an undisclosed target in its "Alnylam 5x15" pipeline that is focused on genetically defined targets and diseases. Arrowhead is eligible to receive from Alnylam milestone payments and royalties on sales of products resulting from the license. In addition, Arrowhead also holds a non-exclusive license from Alnylam to use canonical siRNAs in oncology, respiratory diseases, metabolic diseases and certain liver diseases. This includes a sub-license from Isis Pharmaceuticals (Nasdaq/ISIS/NR) giving Arrowhead license for siRNA chemical modifications for these specific disease areas. Alnylam is a \$1.2 billion (market capitalization) biotechnological company with a number of pipeline programs and partnerships, which began this year with over \$220 million in cash and recently completed a \$174 million public offering of stock.

Cyclosert-Tubulysin Conjugate (Tube Pharmaceuticals GmbH)

Arrowhead has a license and joint development agreement with privately-held Vienna, Austria-based biotech firm Tube Pharmaceuticals, which gives Tube the right to develop Cyclosert-enabled tubulin inhibitors. Tubulysins are a novel tubulin-targeted class of natural compounds with potent antiproliferative activity against multiple cancer types. Tube Pharma is conducting preclinical studies. Arrowhead is eligible to receive milestones and royalties on sales.

Homing Peptides Discovery (Merck)

In August 2012, Arrowhead signed an agreement with Merck (NYSE/MRK/NR) to undertake an evaluation of a novel proprietary therapeutic monoclonal antibody candidate derived from Arrowhead's human-derived peptide targeting and discovery program. Under the agreement, Merck will bear the costs involved in evaluating the candidate.

Peptide-Drug Conjugates (Shire plc)

In December 2012, Arrowhead signed a research collaboration and license agreement with Shire plc (Nasdaq/SHPG/NR), to develop and commercialize targeted peptide-drug conjugates (PDCs) by utilizing Arrowhead's human-derived Homing Peptide platform and Shire's therapeutic payloads. Arrowhead will receive research funding and could be eligible for development, regulatory, and commercialization milestone payments of up to \$32.8 million for each development candidate, plus additional milestone payments for a second potential indication, and royalties on worldwide sales. Under the agreement, Arrowhead will identify peptides that selectively bind and internalize in an undisclosed tissue type and that are capable of delivering a therapeutic payload to that tissue. The Company will receive funding for its internal and external research program-related costs and Shire will have an option to obtain an exclusive license to develop and commercialize a therapeutic agent targeted by the designated peptides and be responsible for clinical development and commercialization of products arising from the collaboration. Shire's HGT (Human Genetic Therapies) division, based in Lexington, Massachusetts, focuses on novel therapies to treat life-threatening genetic diseases.

Operations

As part of the October 2011 acquisition of Roche's RNA therapeutics business, Arrowhead operates a research and development facility in Madison, Wisconsin. This facility was originally built and equipped by Roche. Since the 2011 acquisition, Arrowhead has integrated other development operations into that facility, including work on platforms RONDEL, DPCs, Homing Peptides, and clinical candidates CALAA-01, Adipotide, and ARC-520. A summary of the facility is provided below:

- Approximately 40 scientists;
- State-of-the-art laboratories: 24,000 total sq. ft. of lab space;
- Complete small animal facility with capacity for 10,000 rodents in 2012;
- Primate colony housed at University of Wisconsin;
- In-house histopathology capabilities;
- Animal models for metabolic, viral, and oncologic diseases;
- Animal efficacy and safety assessment;
- Peptide synthesis and analytics capabilities;
- Polymer and small molecule synthesis and analytics capabilities (NMR, mass spec, etc.);
- Polymer and siRNA PK, biodistribution, clearance methodologies; and
- Confocal microscopy, flow cytometry, Luminex (Nasdaq/LMNX/NR) platform, clinical chemistry analytics.

The Company also maintains administrative offices in Pasadena, California.

Intellectual Property

Arrowhead controls approximately 154 issued patents (including European validations) and 292 patent applications. The pending applications have been filed throughout the world, including in the United States, Australia, Canada, Europe, and various countries in Asia and Latin America. Related to the RONDEL and Cycloset drug delivery platforms, Arrowhead controls 55 patents including approximately 34 patents covering linear cyclodextrin copolymers utilized in RONDEL and CYCLOSERT, and approximately 14 patents directed to inclusion complexes and drug-cyclodextrin complexes utilized in these two platforms. Approximately seven additional patents issued in the United States and Europe are directed to supramolecular complexes containing therapeutic agents. Arrowhead's Calando subsidiary also owns a U.S. issued patent (in addition to 14 patents in Europe) directed to the siRNAs targeting the gene targeted by the active ingredient in CALAA-01, as well as a U.S. patent directed to the siRNA active ingredient of CALAA-02. The Company also controls 18 patents related to the Homing Peptide platform and related to Adipotide, a drug candidate for the treatment for obesity and related metabolic disorders. Approximately five of these patents are United States patents and the remaining patents are validated in European jurisdictions. In addition, the Company controls eleven patents related to the Dynamic Polyconjugate drug delivery platform and approximately 41 patents directed to hydrodynamic nucleic acid delivery. With the exception of certain patents related to various iterations of Hydrodynamic delivery which expire in 2015, the Company's patents hold expiration dates between 2018 and 2031.

Recent Results and Balance Sheet/Cash Flow

Earlier this month, Arrowhead Research reported operating results for their fiscal first quarter ending December 31st, 2012 and filed their Q1/2013 10Q report with the SEC. For the quarter, the Company recorded \$159,000 in revenue, an increase from \$24,000 in Q1 2012, primarily from license agreements and service revenue related to the Roche Madison acquisition. Total operating expenses for the three months ended December 31, 2012 were \$5.0 million, compared to \$4.1 million for the three months ended December 31, 2011, primarily due to a full three months of activity at the Madison facility as well as higher R&D costs related to clinical development, manufacturing and toxicology testing of ARC-520. After other expenses, the net loss to Arrowhead was \$4.6 million or (\$0.33) per share in Q1/2013 as compared with a net loss of \$2.5 million or (\$0.25) per share in Q1/2012, which included a one-time gain of \$1.6 million on the purchase of the Roche Madison assets. During the first quarter, net operating cash used by Arrowhead was \$3.8 million, as compared with net cash operating outflow of \$2.7 million in Q1/2012.

At the end of the first quarter, Arrowhead held \$2.9 million in cash, as compared to \$3.4 million at the start of the quarter, however, subsequent to the end of the first quarter the Company was able to add an additional \$3.3 million in cash proceeds to the balance sheets as a result of an equity offering. In addition, as a result of a transaction completed in January 2013 related to a note receivable from Wisepower (related to former subsidiary Unidym), the Company expects to receive an additional \$2.5 million in cash by the end of the second fiscal quarter 2013 (ending March 2013).

Outlook/Growth Drivers

We estimate that Arrowhead Research will incur operating losses of approximately \$17 million or (\$1.00) per share in fiscal 2013 (ending September), based on 16.8 million weighted average shares outstanding for the year. Our estimates assume operating expenses for the fiscal year similar to those incurred in the first fiscal

quarter on an annualized basis, and increased revenues versus fiscal 2012 primarily due to a full year of activity at the recently acquired Roche Madison facility. After considering approximately \$3.4 million in non-cash charges and expenses, including stock option compensation expense and patent-related costs, we are estimating that Arrowhead will incur approximately \$13 million in operating cash burn in fiscal 2013E. Our estimate does not assume the receipt of any significant initial licensing fees or milestone payments from potential new partnerships signed as the year progresses.

In later years, however, we are forecasting that licensing fees, milestone payments, service revenues for discovery contracts, and further down the road product sales royalties will increase for Arrowhead, and although we also foresee costs increasing moderately each year (10% annually), the significant high-margin gross profits accruing to the Company from these fees (we are not assuming the build-out of an internal sales force) should allow the Company to significantly reduce losses and operating cash burn. Our financial forecasts for Arrowhead Research are including at the end of this report.

Catalysts/Investor Timeline

- 1) Webcast focusing on ARC-520 development and HBV market – March 2013
- 2) Webcast on new DPC constructs and tumor targeting structures – Calendar Q2/2013
- 3) Publications in peer-reviewed scientific journals on DPCs and Peptide targeting – Calendar 2013
- 4) Start of treatment of healthy volunteers (Australia most-likely) with ARC-520 – Calendar Q3/2013
- 5) Start of treatment for ARC-520 in chronic HBV patients (Hong Kong) – End of Calendar 2013
- 6) Interim results for Phase 1 trial Adipotide in PCRC patients – End of Calendar 2013
- 7) Progress of partner-based programs with Cerulean (Phase 2) and Shire (Peptide discovery) – 2013
- 8) Announcement of new PDC and RNAi clinical candidates – 2013

Management

Christopher Anzalone, Ph.D. has been President, Chief Executive Officer and Director of the Company since December 1, 2007. In 2005, Dr. Anzalone formed and served as CEO of the Benet Group LLC, a private equity firm focused on creating and building new nano-biotechnology companies from university-generated science. While at The Benet Group, Dr. Anzalone was founding CEO in two portfolio companies, Nanotope, a tissue regeneration company, and Leonardo Biosystems, an oncology drug delivery company. Dr. Anzalone remains CEO and director of Nanotope. Dr. Anzalone is a director of Arrowhead's wholly-owned subsidiary, Arrowhead Madison Inc., majority-owned subsidiaries, Calando Pharmaceuticals, Inc., Ablaris Therapeutics, Inc., and Tego Biosciences Corporation and minority investment, Leonardo Biosystems, Inc. Prior to his tenure at Benet Group, from 1999 until 2003, he was a partner at the Washington, DC-based private equity firm Galway Partners, LLC, where he was in charge of sourcing, structuring, and building new business ventures and was founding CEO of NanoInk, Inc., a leading nanolithography company. Dr. Anzalone holds a Ph.D. in Biology from UCLA and a B.A. in Government from Lawrence University.

Kenneth A. Myszkowski, Chief Financial Officer, joined Arrowhead in 2009. Prior to joining Arrowhead, Mr. Myszkowski served as the corporate controller for Broadwind Energy, a public energy company which provides products and services to the wind energy industry. Previous to his position at Broadwind, Mr. Myszkowski was controller for Epcor USA, the U.S. headquarters for Epcor Utilities, Inc., a public energy company. Prior to Epcor, Mr. Myszkowski was controller for two start-up ventures: NanoInk, specializing in Dip Pen

Nanolithography, a nanofabrication technology, and Delphion, which provided on-line tools for intellectual property research. Mr. Myszkowski also held several corporate roles at FMC Corporation and Premark International, both Fortune 500 companies. He began his career in the audit practice of Arthur Andersen & Co. in Chicago, Illinois.. Mr. Myszkowski received his undergraduate degree from the University of Illinois, and his MBA from the University of Chicago Booth School of Business. He is a certified public accountant in the state of Illinois.

Dr. Bruce Given, Chief Operating Officer, joined Arrowhead in 2011. Since October 2009, Dr. Given has been a director of the Company's subsidiary, Calando Pharmaceuticals, Inc., and since February 2010, Dr. Given has been Chief Executive Officer of Leonardo Biosystems, Inc., a company in which Arrowhead holds a minority equity interest. Dr. Given has been a member of the Board of Directors for ICON, plc., a Clinical Research Organization, since 2007. Dr. Given served as the President and Chief Executive Officer, and as a member of the Board of Directors of Encysive Pharmaceuticals, an R&D-based commercial pharmaceutical company, roles he held from 2002 through 2007. Subsequent to his tenure at Encysive until present, Dr. Given has been President of Bruce Given Consulting, a firm that provides consulting services to biotech companies. Prior to his tenure at Encysive, Dr. Given held several senior executive roles at Johnson and Johnson (NYSE/JNJ/NR), Sandoz Pharmaceuticals, and Schering-Plough. Dr. Given obtained his bachelor of sciences degree from Colorado State University and an M.D. from the University of Chicago and completed his medical training at the University of Chicago and at Brigham and Women's Hospital in Boston, where he was a Clinical Fellow at Harvard Medical School. He is board certified in internal medicine and endocrinology and metabolism and has authored 33 scientific publications.

Brendan P. Rae, Ph.D., J.D., joined Arrowhead as Chief Business Officer in November 2011. Prior to joining the Company, Dr. Rae practiced law and worked as a licensing and business development professional in the pharmaceutical and biotechnology industries over the last 15 years. In this capacity, he successfully sourced new products, led due diligence and commercial evaluation teams, and negotiated and executed agreements in the US, Europe and Far East. Most recently, Dr. Rae was the Chief Business Officer of Vivaldi Biosciences Inc., an influenza vaccine development company headquartered in New York City. Prior to that, he served, from 2005 to 2010, as Senior Vice President, Licensing and Business Development at VIA Pharmaceuticals, Inc., a biotechnology company focused on the development of therapies for the treatment of cardiovascular disease. Dr. Rae's pharmaceutical licensing experience was gained at Hoffman-La Roche Ltd., where he directed the company's in-licensing and out-licensing activities from 1996 to 2003, and at privately-held Purdue Pharma L.P. Dr. Rae has also practiced patent law at the firm of Amster, Rothstein & Ebenstein, LLP. Dr. Rae obtained his Bachelor of Science degree in Microbiology from Glasgow University, and was awarded a Ph.D. by the Institute of Virology in Glasgow, Scotland.. Dr. Rae earned his Juris Doctor degree from Seton Hall Law School in Newark, New Jersey.

Other key management team members at Arrowhead include **Jane Davidson**, currently Vice President, Administration and formerly at Acacia Research Corporation; **Dr. Thomas Schluep**, Vice President, Program Management and formerly of the Canji division of Schering-Plough; **Dr. David Lewis**, Vice President, Biology and Site Head at the Madison facility, and previously the Program Director for RNAi at Mirus Bio Corporation, prior to its acquisition by Roche; and **Dr. David Rozema**, Vice President, Chemistry and formerly a Senior Scientist at Mirus Bio.

In addition to Dr. Anzalone, Arrowhead's Board of Directors includes the following:

Dr. Mauro Ferrari, currently the President and CEO of The Methodist Hospital Research Institute (TMHRI) and the President of The Alliance for NanoHealth; **Edward W. Frykman**, formerly with investment brokerage firms Crowell, Weedon and L.H. Friend; **Dr. Douglass Given**, an Investment Partner at Bay City Capital;

Charles P. McKenney, who maintains a government affairs law practice in Pasadena, California; and **Dr. Michael S. Perry**, currently Global Head, Cell Therapy at Novartis Pharma.

Stock Valuation/Comparables

We have compiled a seven-stock comparison group for Arrowhead Research, selecting companies with clinical programs or marketed products in the Hepatitis B area, such as Gilead Sciences (Nasdaq/GILD/NR) and Idenix (Nasdaq/IDIX/NR); companies employing technologies to create antibody-drug conjugates or small molecule-drug conjugates for oncology therapeutics including Endocyte (Nasdaq/ECYT/NR), Immunogen (Nasdaq/IMGN/NR) and Seattle Genetics (Nasdaq/SGEN/NR) and finally several firms in the RNAi area, such as Arrowhead's partner Alnylam as well as Tekmira (Nasdaq/TKMR/NR). The comparison, shown below, portrays Arrowhead's shares as undervalued vis-à-vis the comparable group in terms of both stock appreciation over the past 12 months (a decline of 57% for ARWR as compared with an increase of 55% on average for the group) and enterprise value, at only \$36 million for ARWR versus an average of over \$10 billion and minimum of \$57 million for the group, despite having many of the same partners.

Table 1. Drug Discovery Comparable Company Analysis

Company	Symbol	Current Price	Shares (millions)	Market Cap (\$Millions)	Enterprise Value	Stock Price	52-Week Gain/Loss	Notes
					(\$Mill)	2/27/2012		
Alnylam	ALNY	\$23.85	52.5	\$1,252.1	\$1,026.1	\$13.58	75.6%	Leader in RNAi therapeutics
Endocyte	ECYT	\$8.70	35.9	\$312.3	\$155.0	\$3.61	141.0%	Small molecule-drug conjugates for cancer
Gilead Sciences	GILD	\$42.06	1,520.0	\$63,900.0	\$68,740.0	\$22.60	86.1%	HBV and HIV therapeutics
Idenix	IDIX	\$4.36	133.9	\$583.8	\$331.9	\$12.56	-65.3%	HBV and HCV therapeutics
Immunogen	IMGN	\$14.62	84.2	\$1,231.0	\$1,020.0	\$13.97	4.7%	Antibody-drug conjugates for cancer
Seattle Genetics	SGEN	\$26.86	119.3	\$3,204.4	\$2,840.4	\$17.57	52.9%	Antibody-drug conjugates for cancer
Tekmira	TKMR	\$4.51	14.0	\$63.1	\$57.5	\$2.40	87.9%	Canadian-based RNAi developer
Average					\$10,595.9		54.7%	
Arrowhead Research	ARWR	\$2.27	17.3	\$39.3	\$36.3	\$5.24	-56.7%	RNAi and Peptide drug development

Source: Dawson James Securities, CapitalIQ

We have also undertaken a Discounted Cash Flow (DCF) analysis for Arrowhead in order to determine valuation, focusing on future prospects for the Company's lead pipeline products ACT-520 for HBV and Adipotide for Obesity as well as potential revenues from development and drug discovery partnerships. Using potential cash flows up to fiscal 2020E, a long-term discount factor of 30%, and current shares outstanding of 17.3 million we estimate that Arrowhead shares can be valued at approximately \$70 million, thus we are initiating shares of AWRW with a Buy rating and 12-18 month price target of \$4 per share.

Risk Factors

In addition to normal economic and market risk factors that impact most equities and the common risks shared by Arrowhead with other companies in the industry, we believe an investment in Arrowhead Research involves the following risks:

- **FDA and regulatory risks** – Arrowhead is subject to regulatory review for its ongoing research and development activities, principally the US Food and Drug Administration but also potentially with other international regulatory agencies as well.
- **Reliance on joint venture partners** — At present, Arrowhead has a number of partnership agreements signed in both the development and drug discovery areas. Partnerships and joint ventures bring certain risks that are not present in internal operations, such as potential delays, company disagreements, or

unforeseen financial difficulties at the partnering entity, and there can be no assurance that these partnerships will prove to ultimately successful.

- **Need to defend patents and other intellectual property** – At present, Arrowhead holds a large number of patents in the US and in foreign jurisdictions with additional patents pending in the US and internationally related to drug delivery platform technologies and processes. The Company may need to defend its patents in the US and overseas in the future, particularly if one or more products receive regulatory approval and are successfully marketed.
- **Need to raise additional capital** - Currently, Arrowhead has enough cash on hand to fund ongoing research and marketing development programs through the end of fiscal 2013, approximately. However, the Company does not have a history of profitable operations and unforeseen events including potential delays in regulatory approvals could require Arrowhead to raise additional capital through the sale of equity within a shorter time-frame, therefore potentially diluting current shareholders.
- **Limited stock liquidity** – Trading volume in Arrowhead stock is comparatively light. As such, news regarding Arrowhead, its target market, partners and/or competitors could lead to significant volatility in the stock price.
- **Competitive Markets** – The Company will potentially compete in its target pharmaceutical markets with a number of other large multi-national manufacturers, generic drug companies, and specialty pharma firms, some of which represent much larger companies. There can be no assurance that the Company will be able to successfully launch new products into these competitive markets in the future.
- **Recent acquisition activity** – Over the past several years, Arrowhead has completed several major acquisitions. These acquisitions will require the Company to integrate existing operations and staff over time, and there can be no assurance that Arrowhead management will be able to avoid unforeseen problems with past (or future) acquisitions. In addition, several of these acquisitions were completed at least in part through the issuance of common stock in Arrowhead, which can be dilutive and harmful to trading activity in certain cases should these shares come out into the market in a non-orderly fashion.

Arrowhead Research Coporation
Consolidated Statements of Income
(in \$000s, except EPS)

Robert M. Wasserman

Fiscal Year Ending September	2011	2012	2013E	2014E	2015E	2016E
Revenues						
Discovery and service contracts	\$296.1	\$146.9	\$2,000.0	\$4,000.0	\$5,000.0	\$6,000.0
Product sales royalties and regulatory milestones	<u>0.0</u>	<u>0.0</u>	<u>0.0</u>	<u>5,000.0</u>	<u>30,000.0</u>	<u>50,000.0</u>
Total revenues	<u>296.1</u>	<u>146.9</u>	<u>2,000.0</u>	<u>9,000.0</u>	<u>35,000.0</u>	<u>56,000.0</u>
Expenses						
Salaries and payroll-related costs	1,408.4	6,414.9	6,400.0	6,900.0	7,400.0	7,900.0
General and administrative and other	3,795.4	6,439.3	3,700.0	4,000.0	4,300.0	4,600.0
Research and development	3,277.8	5,391.5	6,000.0	6,300.0	6,600.0	6,900.0
Other, non-cash and one-time charges	<u>1,644.9</u>	<u>2,990.4</u>	<u>3,400.0</u>	<u>3,700.0</u>	<u>4,000.0</u>	<u>4,300.0</u>
Total operating expenses	<u>10,126.4</u>	<u>21,236.1</u>	<u>19,500.0</u>	<u>20,900.0</u>	<u>22,300.0</u>	<u>23,700.0</u>
Loss from operations	(9,830.3)	(21,089.2)	(17,500.0)	(11,900.0)	12,700.0	32,300.0
Interest expense, net	86.5	36.0	30.0	30.0	500.0	1,000.0
Other expense, net	<u>6,251.3</u>	<u>(1,057.5)</u>	<u>(50.0)</u>	<u>(50.0)</u>	<u>(50.0)</u>	<u>(50.0)</u>
Net income (loss)	(3,492.4)	(22,110.7)	(17,520.0)	(11,920.0)	13,150.0	33,250.0
Non-controlling interests	<u>363.5</u>	<u>984.8</u>	<u>600.0</u>	<u>600.0</u>	<u>600.0</u>	<u>600.0</u>
Net income (loss) attributable to common stock	<u>(3,128.9)</u>	<u>(21,125.9)</u>	<u>(16,920.0)</u>	<u>(11,320.0)</u>	<u>13,750.0</u>	<u>33,850.0</u>
Basic and diluted income (loss) per share	<u>(\$0.44)</u>	<u>(\$1.90)</u>	<u>(\$1.01)</u>	<u>(\$0.59)</u>	<u>\$0.62</u>	<u>\$1.34</u>
Basic and diluted shares outstanding	7,181.1	11,129.8	16,800.0	19,300.0	22,300.0	25,300.0
Key ratios:						
Cash Flow/share	(\$1.13)	(\$1.62)	(\$0.84)	(\$0.42)	\$0.77	\$1.49

Balance Sheets

(\$000s)

<i>Assets:</i>	9/30/12	12/31/12
Cash and marketable securities	\$3,483.8	\$2,987.0
Receivables	19.3	124.6
Prepaid expenses	618.1	460.9
Note receivable, net	<u>2,446.1</u>	<u>2,491.5</u>
Total current	6,567.3	6,064.0
Property & equip., net	4,895.7	4,426.7
Intangible assets and other long-term	<u>5,064.8</u>	<u>4,740.5</u>
TOTAL ASSETS	16,527.8	15,231.1
<i>Liabilities:</i>		
Accounts payable	878.0	809.5
Accrued expenses	1,858.0	1,910.4
Deferred revenue	37.5	109.375
Notes payable	100.0	935.3
Other current	<u>2,454.4</u>	<u>2,313.3</u>
Total current	5,327.9	6,078.0
Notes payable, long-term	839.4	50.0
Other long-term	1,551.6	1,498.7
Stockholders' equity (deficiency)	<u>8,808.9</u>	<u>7,604.5</u>
TOTAL LIAB & EQ	16,527.8	15,231.1

Source: Dawson James Securities, Inc. estimates; Company documents

Important Disclosures:

Price Chart:



Price target and ratings changes over the past 3 years:

Initiated – February 26, 2013 – Price Target \$4.00

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- 1) **Buy:** the analyst believes the price of the stock will appreciate and produce a total return of at least 20% over the next 12-18 months;
- 2) **Neutral:** the analyst believes the price of the stock is fairly valued for the next 12-18 months;
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The following chart reflects the range of current research report ratings for all companies followed by the analysts of the Firm. The chart also reflects the research report ratings relating to those companies for which the Firm has performed investment banking services.

	Company Coverage		Investment Banking	
Ratings Distribution	# of Companies	% of Total	# of Companies	% of Totals
Market Outperform (Buy)	14	88%	9	64%
Market Perform (Neutral)	2	13%	0	0%
Market Underperform (Sell)	0	0%	0	0%
Total	16	100%	9	56%

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