ARROWHEAD RESEARCH CORP
Form 10-K
December 28, 2012

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended September 30, 2012.

¨ **TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number 000-21898

ARROWHEAD RESEARCH CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**46-0408024**
(State of incorporation)	**(I.R.S. Employer Identification No.)**

225 S. Lake Avenue, Suite 1050

Pasadena, California 91101

(626) 304-3400

(Address and telephone number of principal executive offices)

Securities registered under Section 12(b) of the Exchange Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	The NASDAQ Capital Market

Securities registered pursuant to Section 12(g) of the Exchange Act:

None

Indicate by a check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by a check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer ¨	Smaller Reporting Company x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No x

The aggregate market value of issuer s outstanding Common Stock held by non-affiliates was approximately $68 million based upon the bid price of issuer s Common Stock on March 31, 2012. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding Common Stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of December 21, 2012, 15,644,158 shares of the issuer s Common Stock were outstanding.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, and we intend that such forward-looking statements be subject to the safe harbors created thereby. For this purpose, any statements contained in this Annual Report on Form 10-K except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as may, will, expect, believe, anticipate, intend, could, estimate, or continue or the negative or other variations thereof or comparable terminology are intended to identify forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our businesses, or other characterizations of future events or circumstances are forward-looking statements.

The forward-looking statements included herein are based on current expectations of our management based on available information and involve a number of risks and uncertainties, all of which are difficult or impossible to predict accurately and many of which are beyond our control. As such, our actual results may differ significantly from those expressed in any forward-looking statements. Factors that may cause or contribute to such differences include, but are not limited to, those discussed in more detail in Item 1 (Business) and Item 1A (Risk Factors) of Part I and Item 7 (Management s Discussion and Analysis of Financial Condition and Results of Operations) of Part II of this Annual Report on Form 10-K. Readers should carefully review these risks, as well as the additional risks described in other documents we file from time to time with the Securities and Exchange Commission. In light of the significant risks and uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by us or any other person that such results will be achieved, and readers are cautioned not to place undue reliance on such forward-looking information. Except as may be required by law, we disclaim any intent to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

PART I

ITEM 1. BUSINESS

Description of Business

OVERVIEW

Arrowhead Research Corporation is a clinical stage targeted therapeutics company with development programs in oncology, obesity, and chronic hepatitis B virus infection. Arrowhead is focused on creating new therapeutics that are preferentially taken up by target tissues in order to maximize a drug s efficacy and potentially limit side effects associated with exposure to healthy cells. Arrowhead has assembled a broad set of technologies and licenses to enable targeted RNAi therapeutics capable of silencing specific gene products in specific cells. Arrowhead has also assembled a proprietary targeting library that may be used with its RNAi platforms as well as with small molecule or peptide drugs. These platforms have yielded several drug candidates under both internal and partnered development.

Lead Product Candidates

Adipotide® is an anti-obesity peptide that has been shown to promote weight loss in animal models. It is the first drug candidate from Arrowhead s Homing Peptide platform and entered a phase 1 clinical trial in 2012.

ARC-520 is an RNAi-based therapeutic designed to treat chronic hepatitis B virus (HBV) infection. It is the first drug candidate from Arrowhead s Dynamic Polyconjugate® siRNA delivery platform and is expected to enter clinical trials in 2013.

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.

Platform Technologies

The Dynamic Polyconjugate® (DPC®) platform is a small RNA delivery system that may be targeted to address multiple organ systems and cell types. It 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, induce efficient endosomal escape, and has wide safety margins using a variety of siRNA molecules.

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

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

Primary Strategic Opportunities

Delivering siRNA

RNA interference (RNAi) is a naturally occurring mechanism that effects gene expression. Short interfering RNAs (siRNAs) have been shown to trigger RNAi and are thought to be a potentially powerful and specific way of silencing expression of disease-causing gene products. However, the lack of effective and safe delivery has impeded progress of the field. Arrowhead has multiple polymer-based, non-lipid delivery

systems that enable development of RNAi therapeutics. Importantly, Arrowhead s delivery systems have been validated in multiple species and have demonstrated high levels of efficiency and specificity with wide safety margins.

Enabling Targeted Drugs

Examples of guided therapeutics producing positive patient outcomes are rapidly emerging. Arrowhead s human-derived targeting library, comprised of over 42,000 peptides, is being mined to create PDCs designed to home specifically to target cells. PDCs have the potential to produce the advantages of antibody drug conjugates while bringing new benefits such as ease of manufacturing.

Patient Population Enrichment Strategies

Arrowhead s targeting library can be used for companion diagnostics that identify patient populations most likely to respond to a particular treatment, thus moving toward more personalized medicine.

Improving Generics

Arrowhead s targeting library can be used to make PDCs with generics designed to have an improved efficacy and safety profile as compared to untargeted counterparts.

Arrowhead s internal drug pipeline is intended to drive value directly through the development of novel therapeutics and to provide proof of concept for the platform technologies. We actively seek collaboration and licensing agreements with leading biopharmaceutical companies to augment their pipelines through the application of our technologies and to advance the development and commercialization of our own technology platforms and drug candidates. Partnerships are intended to provide access to external expertise and capital to complement our internal development and create commercialization opportunities in areas outside of our core focus.

RECENT EVENTS

Fiscal 2012 brought substantial change to Arrowhead. We have executed on our long-term strategy of transitioning from a nanotechnology holding company in multiple industries to a focused biotech model. We are now a unified therapeutics company developing actively guided drugs that interact preferentially with target tissues based on broad RNAi and peptide targeting technology platforms.

Arrowhead made two acquisitions in fiscal 2012. These acquisitions included new technology platforms, R&D infrastructure and expertise, and operating and business development management. We believe these acquisitions provide us with a solid foundation to discover and develop drug candidates and support partnerships that we expect will drive long-term value for our shareholders. Some of the key steps in this transformation were:

Acquired the RNAi therapeutics business assembled by Roche, which provided us with the following:

- siRNA delivery technologies, the most advanced of which is Dynamic Polyconjugates (DPCs);
- License to multiple siRNA structures and chemistries in key therapeutic areas;
- A state-of-the-art 24,000 square foot R&D facility with complete small animal facilities;
- R&D staff of 40 scientists; and
- Multiple pre-clinical drug development programs, including an siRNA therapeutic for chronic hepatitis B infection, which is approaching an IND filing as ARC-520.

Acquired Alvos Therapeutics, Inc. providing Arrowhead with a library of peptide targeting sequences used to create PDCs as well as intellectual property that can be used to generate novel targeting antibodies;

Augmented our management team by hiring accomplished biopharma executives Bruce Given, M.D. as Chief Operating Officer and Head of R&D, and Brendan Rae, Ph.D., J.D., as Chief Business Officer;

Created a centralized infrastructure for the management of clinical trials; and

Integrated and consolidated R&D operations in the Madison facility, including work on the RONDEL siRNA delivery system and CALAA-01 candidate, our suite of obesity/metabolic disease compounds including the Adipotide candidate, and the Homing Peptide discovery and development programs;

These steps have created an integrated development operation that allows Arrowhead to advance multiple programs simultaneously. Since our drug development strategy is unified around actively targeted delivery, our R&D operations are synergistic across drug candidates and platforms. Additionally, Arrowhead now has the infrastructure, expertise, IP portfolio, and management that we believe is necessary to attract and support a broad range of partnerships and research collaborations with large biopharma companies from discovery stage through clinical trials.

PIPELINE OVERVIEW

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

Internal Clinical Programs

ARC-520 Hepatitis B Virus Infection

According to the World Health Organization, 360 million people worldwide are chronically infected with hepatitis B virus, of which 500,000 to 1,000,000 people die each year from HBV related liver disease. 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, the infected person 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, 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. 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 severe flu-like symptoms, marrow suppression, and autoimmune disorders.

We see the 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. We believe a novel 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 an siRNA therapeutic intended for delivery to the active site of infection using our 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. We have designed ARC-520 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.

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. We are currently conducting IND-enabling studies with a goal to enter a Phase 1 clinical study in 2013.

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.

An Investigational New Drug Application (IND) for Adipotide was filed with the FDA, and we began enrolling patients in 2012 as part of a Phase 1 clinical trial to test the safety of the compound in human patients. Our 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.

Potential Advantages of Adipotide:

- Shown to promote weight loss of 11% to 30% of total body mass in preclinical studies using rodents and spontaneously obese rhesus monkeys after just 28 days of treatment;
- Shown to reduce abnormalities in blood chemistry associated with diabetes;
- Novel mechanism of action compared to other known therapeutics on the market or in clinical trials;
- No modulation of neurotransmitters seen in pre-clinical studies, thus unlikely to have psychological side effects;
- No amphetamine-like mechanism of action and thus unlikely to yield GI side effects.

Adipotide is based on Arrowhead s Homing Peptide library developed at 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 our majority-owned subsidiary, Ablaris Therapeutics, Inc. (Ablaris). Arrowhead owns 64% of the fully diluted shares of Ablaris.

CALAA-01 Solid Tumors

CALAA-01 is a combination of our RONDEL delivery technology 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, and thus tumor growth. The internally developed siRNA demonstrates potent anti-proliferative activity across multiple types of cancer cells. CALAA-01 was the first siRNA therapeutic candidate to target cancer in a human clinical study

and we believe was also the first successful systemic delivery of an siRNA therapeutic candidate.

In August 2012 enrollment into the Phase 1 clinical trial was completed. Adverse events observed coincided with an increase in certain cytokine levels. Elevation in cytokines is consistent with an acute immune response to the natural siRNA used in CALAA-01. These reactions also appeared to be transient, such that if a patient stayed on CALAA-01, the cytokine responses often subsided. Based on these results, a Phase 1b trial was initiated using a modified dosing schedule in which patients were pretreated with a lower dose to assess whether this strategy can increase patient safety and further increase the maximum tolerated dose. Patient enrollment was completed in August 2012 and analysis of final study data is being prepared.

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/m^2) 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 our 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.

Partnered Programs

Cyclosert and CRLX-101 (formerly IT-101)

The linear cyclodextrin-based drug delivery platform, Cyclosert, was designed for the delivery of small molecule drugs. In December 2008, we completed a Phase 1 trial with IT-101, a conjugate of the linear cyclodextrin polymer and Camptothecin, a potent anti-cancer drug, with a positive safety profile and indications of efficacy.

In June 2009, we entered into a transaction with Cerulean Pharmaceuticals, Inc., a privately-held Boston, Massachusetts based company. Cerulean licensed rights to further research and commercialize IT-101 (now known as CRLX-101), and the Cyclosert platform for all products except for nucleic acids, tubulysin, cytolysin and second generation epothilones. In connection with the transaction, we assigned certain patents to Cerulean and Cerulean granted back to us rights necessary to research and commercialize the excluded products. As such, we retain the rights to the RONDEL siRNA delivery platform, as well as CALAA-01.

We 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, we are entitle 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.

Tubulin Inhibitor

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

Alnylam Pharmaceuticals

In January 2012, Arrowhead granted Alnylam Pharmaceuticals, Inc., (Alnylam) a license to utilize the Dynamic Polyconjugate delivery technology for a single RNAi therapeutic product. Alnylam is collaborating with Arrowhead to develop this technology for an undisclosed target in its Alnylam 5x15 pipeline, which is focused on genetically defined targets and diseases. Arrowhead is eligible to receive milestone payments and royalties on sales from Alnylam.

Shire

In December 2012, Arrowhead signed a research collaboration and license agreement with Shire AG to develop and commercialize targeted peptide-drug conjugates (PDCs) utilizing Arrowhead s human-derived Homing Peptide platform and Shire s therapeutic payloads. Arrowhead may 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 indication, and royalties on worldwide sales.

Preclinical Programs

In addition to our clinical candidates and our partner-based programs, we are actively engaged in the discovery and development of additional pre-clinical stage products. We focus on disease targets that are well suited for intervention with guided therapeutics like our PDCs and targeted RNAi therapeutics using our DPC delivery platform. These may include liver disease, oncology, and other therapeutic areas.

RNAI DELIVERY PROGRAM

In October 2011, Arrowhead acquired Roche s RNAi business, including its RNA therapeutic assets, related intellectual property and research facility in Madison, Wisconsin. We believe that these assets position Arrowhead as one of the most advanced and broadest RNAi therapeutics

companies in the world. Arrowhead now possesses the following siRNA assets:

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 giving Arrowhead license for siRNA chemical modifications for these specific disease areas.

Non-exclusive license from City of Hope Comprehensive Cancer Center to Dicer substrate and Meroduplex siRNAs. The Dicer technology may provide advantages over canonical siRNAs in certain circumstances. In addition, different siRNA formats may trigger RNAi more or less efficiently on a target-by-target basis.

Patent estate covering the Dynamic Polyconjugate siRNA delivery system.

Access to certain patents on targeting siRNA drugs with antibodies and small molecules.

State-of-the-art laboratory facilities in Madison, Wisconsin, managed by long term leaders in oligonucleotide therapeutics and delivery, including a small animal research facility and an offsite primate colony.

Intellectual property covering Roche s internally developed liposomal nanoparticle drug delivery technology.

RONDEL siRNA delivery system which has demonstrated gene knockdown in humans in the CALAA-01 clinical trial.

Minority ownership position in Leonardo Biosystems, Inc., a private company developing a multi-stage silicon-based delivery system.

CALAA-01 Phase 1 oncology drug candidate.

We believe this represents one of the broadest siRNA drug technology and delivery portfolios in the world.

RNA Interference & 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 undruggable targets, unlocking the market potential of such targets.

Mechanism of RNA interference

Advantages of RNAi as a Therapeutic Modality

Silences the expression of disease causing genes;

Potential to address any target in the transcriptome including previously undruggable targets;

Rapid lead identification;

High specificity;

Opportunity to use multiple RNA sequences in one drug product for synergistic silencing of related targets; and

siRNAs are uniquely suited for personalized medicine through target and cell specific delivery and knockdown.

Addressing the siRNA Delivery Challenge

To date, the primary challenge to 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.

To address the delivery challenge, Arrowhead has a leading team of researchers with extensive siRNA therapeutic know-how and two validated delivery platforms:

- The Dynamic Polyconjugate system is an amphipathic polymer to which shielding agents and targeting ligands are reversibly attached.

- The RONDEL™ delivery system utilizes targeted cyclodextrin polymers to deliver siRNA and other oligonucleotides to tumors. Human *in vivo* gene knockdown has been demonstrated in a Phase 1 cancer trial, establishing human proof of concept for the RONDEL system.

These are both modular systems that may be optimized on a target-by-target basis. Importantly, they also may be targeted to address a variety of tissues.

The Dynamic Polyconjugate 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 by our scientists in Madison, Wisconsin, 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 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 of target gene expression. This lytic 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.

- Inhibition of non-specific interactions with blood components and non-targeted cell types.

Arrowhead has developed multiple forms of the prototypical DPC delivery system. Our ARC-520 clinical candidate utilizes a formulation where the siRNA is conjugated to cholesterol and is not attached to the DPC. Pre-clinical studies have shown 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.

DPCs using 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 is observed at low siRNA doses with limited toxicity in rodents and non-human primates. Arrowhead 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. PK and biodistribution studies indicate that the new masking technology is highly stable, allowing for maximal bioavailability and long circulation times. Arrowhead is developing this formulation for use in multiple therapeutic areas including oncology.

RONDEL Delivery System

For this delivery system, polymers form the foundation for a 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 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 the 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.

RONDEL Nanoparticle

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. We believe 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. The drug delivery system has the added benefits of increasing solubility and allowing 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.

Any siRNA sequence can be easily substituted Because RONDEL binds to the siRNA backbone, other siRNAs 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 We have demonstrated successful delivery of functional siRNA therapeutics to tumor cells and to hepatocytes by systemic administration and confirmed sequence-specific gene inhibition.

Human proof of concept CALAA-01, the first clinical candidate developed using the RONDEL system, has established several important firsts in human testing of an 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 subsidiary, Calando Pharmaceuticals, Inc. (Calando). Arrowhead owns 74% of the fully diluted shares of Calando.

HOMING PEPTIDE PROGRAM

In April 2012, Arrowhead acquired Alvos Therapeutics, Inc. (Alvos). Alvos licensed a discovery platform and large library of proprietary human-derived Homing Peptides from the MD Anderson Cancer Center. This discovery platform is designed to identify targeting agents, such as peptides, that selectively accumulate in primary and metastatic tumors, associated vasculature, and to 30 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 others. This new platform was acquired because it fit well into our existing business. One of the key advantages of our RNA delivery systems is their ability to be targeted. With a vast proprietary targeting library of our own, we believe that we can enhance the value of our RNAi programs and differentiate our capabilities from those of our competitors. In addition, we believe that we 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.

This 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. Our proprietary library of 42,000 unique targeting sequences can be used with our 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 this technology, run 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 would 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 our knowledge, they are the only group in the world 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 our proprietary siRNA delivery vehicles. Our 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 our targeted therapeutic program with a powerful 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 we can potentially transform a therapeutic that interacts with most cells in the body into one that interacts preferentially with the cell of choice. We believe that this transition from untargeted to targeted drugs is a paradigm shift for cancer therapeutics and that our new library puts us at the forefront of this transformation. We intend to build our own pipeline and work with partners to apply our targeting sequences to their drugs. We believe that this specific targeting will enable us to make existing generics safer and more effective and we intend 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 we now have, 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. 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.

We believe 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.

Intellectual Property

We control 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, Argentina, Australia, Brazil, Canada, Chile, China, Europe, the Arab States of the Gulf, Israel, India, Japan, Republic of Korea, Mexico, Peru, Philippines, Russian Federation, Singapore, Thailand, Taiwan and Venezuela.

RONDEL

Calando controls an intellectual property portfolio of patents directed to certain linear cyclodextrin polymers and related technology (the Linear Cyclodextrin System). The portfolio is directed to both RONDEL and Cyclosert. In June 2009, Calando sold and assigned to Cerulean certain patents (Cerulean Assigned Patents) directed toward linear cyclodextrin polymers conjugated to drugs. Additionally, Calando granted Cerulean an exclusive license under its rights to the Linear Cyclodextrin System to develop and commercialize CRLX-101 and Cerulean Products. Calando retained rights to use the Linear Cyclodextrin System to develop drugs in which a therapeutic agent is (i) a nucleic acid (e.g., siRNA), (ii) a second generation epothilone, (iii) tubulysin or (iv) cytolysin (collectively, the Calando Products).

The issued patents include approximately 55 patents directed to the RONDEL and CYLCOSERT drug delivery platforms. Included in these 55 patents are approximately 34 patents covering linear cyclodextrin copolymers utilized in RONDEL and CYCLOSERT, issued in the United States, Europe (Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, the United Kingdom, Greece, Ireland, Israel, Italy, Luxembourg, Monaco, Netherlands, Portugal, Sweden), Australia, Brazil, Canada, China, Cyprus, Japan, Republic of Korea, Mexico, Russian Federation, Singapore and South Africa. Approximately 14 patents are directed to inclusion complexes and drug-cyclodextrin complexes utilized in the RONDEL and CYLCOSERT platforms. These patents have issued in the United States, Australia, China, Israel, Japan, Republic of Korea, Russian Federation, Singapore, Taiwan and South Africa. Approximately seven additional patents issued in the United States and Europe (Austria, Switzerland, Germany, France and the United Kingdom) are directed to supramolecular complexes containing therapeutic agents.

Calando also owns a U.S. issued patent (in addition to 14 patents in Europe, i.e., Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, the United Kingdom, Hungary, Italy, Netherlands, Poland and Sweden) 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.

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HOMING PEPTIDES

We also control 18 patents related to our Homing Peptide platform, related to Adipotide, our 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 Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Ireland, Greece, Italy, Netherlands, Portugal, Sweden and Turkey.

DPC S

In addition, we control eleven patents related to our Dynamic Polyconjugate drug delivery platform. These patents have issued in the United States, Australia, Canada, India, Mexico, Russia and South Africa. We also control approximately 41 patents directed to hydrodynamic nucleic acid delivery which issued in the United States, Australia and Europe (Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, the United Kingdom, Hungary, Ireland, Italy, Netherlands and Sweden).

Thirteen additional patents are directed to various precursors to our DPC delivery platform, and other membrane active polymers, as well as additional drug and gene delivery methodologies and carriers (e.g., lipid- and micelle-based systems).

The approximate year of expiration for each of these various groups of patents are set forth below:

Patent Group	Estimated Year of Expiration
RONDEL and CYCLOSERT	
Linear cyclodextrin copolymers	2018
Inclusion complexes	2021
Drug-cyclodextrin complexes	2024
Supramolecular complexes containing therapeutic agents	2019
CALAA-01	
Patent directed to RRM2 siRNAs	2028
CALAA-02	
Patent directed to HIF-2 alpha (EPAS1) siRNAs	2030
Adipotide®	
Targeting moieties and conjugates	2021
Targeted Pharmaceutical Compositions	2021
Dynamic Polyconjugates® (DPC®)	
Membrane Active Polymers	2027
Membrane Active Polymers Additional Iterations	2024
Copolymer Systems	2024
Polynucleotide-Polymer Composition	2024
Polynucleotide-Polymer Composition Additional Iterations	2031
Polyampholyte Delivery	2017
pH Labile Molecules	2020
Endosomolytic Polymers	2020
Hydrodynamic delivery	
Various iterations	2015
Homing Peptides	
EphA5 Targeting Peptides	2027
IL-11R Targeting Peptides	2022

Calando has licensed patents from Alnylam relevant to siRNA therapeutics for both CALAA-01 and CALAA-02. Calando has out-licensed to Tube Pharmaceuticals GmbH, the use of the linear cyclodextrin system for delivering second generation synthetic epothilone drugs. Calando has also out-licensed to Tube Pharmaceuticals GmbH, the use of the linear cyclodextrin system for delivering tubulysin and cytolysin.

The RNAi and nanoparticle drug delivery patent landscapes are complex and rapidly evolving. As such, we may need to obtain additional patent licenses prior to commercialization of our candidates. You should review the factors identified in Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K.

License Agreements

Cerulean License

The linear cyclodextrin-based drug delivery platform, Cyclosert, was designed for the delivery of small molecule drugs. Cyclosert provides many of the same benefits as the RONDEL system. In December 2008, we completed a Phase 1 trial with IT-101, a conjugate of Calando s linear cyclodextrin polymer and Camptothecin, a potent anti-cancer drug, with a positive safety profile and indications of efficacy.

On June 23, 2009, we entered into a transaction with Cerulean related to Cyclosert and IT-101 (the Cerulean Transaction). In the Cerulean Transaction, we granted Cerulean an irrevocable, perpetual, royalty bearing worldwide license with the right to sublicense, under certain patent rights and know-how in the field of human diseases solely in order to: (a) conduct research and development on the Linear Cyclodextrin System, including making improvements thereto, in order to research and commercialize our clinical asset IT-101 (now known as CRLX-101), as well as certain other products in which no therapeutic agent is specifically defined (the Cerulean Products); (b) research, develop, make, have made, use, market, offer to sell, distribute, sell and import CRLX-101 and Cerulean Products; and (c) use, copy, modify and distribute certain know-how for those purposes. We retained all rights with respect to products in which a therapeutic agent is a (i) tubulysin, (ii) cytolysin, (iii) second generation epothilone or (iv) nucleic acid (hereinafter Calando Products).

The Cerulean Transaction also involved the sale and assignment by us of certain patents directed to Cyclosert and CRLX-101 (the Cerulean Assigned Patents) to Cerulean. Cerulean then granted back to us an exclusive, irrevocable, perpetual, royalty free, worldwide license, with the right to grant sublicenses, under the Cerulean Assigned Patents solely to the extent necessary to research and commercialize products in which each therapeutic agent is a cytolysin, tubulysin, second generation epothilone or any nucleic acid. As such, we retain the rights to the RONDEL siRNA delivery platform, as well as the siRNA-based products, CALAA-01 and CALAA-02.

The Cerulean Transaction resulted in an initial payment to Calando of $2.4 million. Cerulean is obligated to pay development milestone payments of up to $2.75 million if CRLX-101 progresses through clinical trials and receives marketing approval. If approved, we are also entitled to receive up to an additional $30 million in sales milestone payments, plus single digit royalties on net sales. Should Cerulean sublicense CRLX-101 to a third party, we shall 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.

Cerulean is obligated to further pay development milestone payments of up to $3 million for each Cerulean Product that progresses through clinical trials and receives marketing approval. If Cerulean Products are approved, we are entitled to receive up to an additional $15 million in sales milestone payments, plus single digit royalties on net sales. Should Cerulean sublicense a Cerulean Product to a third party, we shall receive a percentage of any sublicensing income at a rate in the tens.

The terms of the agreements of the Cerulean Transactions are tied to the expiration of certain controlled patent rights and Cerulean Assigned Patents. Cerulean may terminate the agreements on thirty (30) days notice and unless there is a drug safety concern, would be obligated to re-assign the CRLX-101 IND back to us and provide us with an exclusive license thereto under the Cerulean Assigned Patents. We are responsible for the costs associated with prosecution of the patents we control and have licensed to Cerulean.

University of Texas MD Anderson Cancer Center License

In December 2010, we obtained an exclusive world-wide license from at the University of Texas MD Anderson Cancer Center in Houston, Texas (UTMDACC) related to Adipotide technology (the UTMDACC License). The UTMDACC License granted us a royalty-bearing, exclusive right (with the right to sublicense) under certain UTMDACC patents to develop and commercialize certain products in the fields of: 1) therapeutics, diagnostics and research services that both (i) incorporate peptides that specifically target adipose tissue, and (ii) are used to treat, diagnose or research solely either (a) obesity, overweight and/or (b) metabolic conditions related to, caused by and/or associated with obesity and overweight, e.g., diabetes; and 2) cancer therapies, diagnostics and research products associated with a specific targeting moiety. We also have rights to certain improvements to the UTMDACC technology arising in the lab of Drs. Wadih Arap and Renata Pasqualini (UTMDACC Improvements).

In consideration for the license, we paid UTMDACC an upfront fee of $2 million and are obligated to pay annual fees initially equal to $50,000 increasing up to a maximum of $100,000, with such annual fees creditable against milestone payments.

We may be obligated to pay development milestone payments of up to $8.3 million for each UTMDCC licensed product that progresses through clinical trials and receives U.S. marketing approval are required. Additional EU and Japanese approval milestone payments are in the low single digit million dollar range. If a commercial drug is developed and approved, royalty payments on net sales of UTMDACC licensed products are in the low single digit range. Should we sublicense or partner a UTMDACC licensed product, UTMDACC would receive partnering fee percentages in the range of single digits to the twenties, depending on the stage of development of the partnered UTMDACC licensed product.

The term of the UTMDACC License is linked to the last to expire patents licensed therein or 15 years if a licensed product contains only licensed know-how. We are obligated to actively and effectively attempt to commercialize the UTMDACC Technology and submit to UTMDACC a Phase 2 clinical trial protocol within two years of obtaining an approved IND. We are also obligated to commence a Phase 2 clinical trial within four years and a Phase 3 clinical trial within seven years of approval of an IND. However, we may obtain yearly extensions of time upon the payment of an increasing fee in the range of tens of thousands of dollars up to several hundred thousand dollars. We also have diligence obligations with respect to any UTMDACC Improvements later added to the license. The UTMDACC license shall automatically terminate if we file for bankruptcy or are unable to pay our bills as they come due.

Research and Development Facility

Arrowhead operates a research and development facility in Madison, Wisconsin. This facility was built and equipped by Roche and was part of our acquisition of their RNA therapeutics business. We have integrated development operations into that facility, including work on our platforms RONDEL, DPCs, Homing Peptides, and our 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;
- Animals 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 platform, clinical chemistry analytics.

Research and Development Expenses

Research and development expenses consist of costs incurred in identifying, developing and testing our product programs. These expenses consist primarily of salaries and related expenses for personnel, license fees, consulting fees, contract research and manufacturing, and the costs of laboratory equipment and facilities. Research and development expense for 2012 was $8.7 million an increase from $3.5 million in 2011, primarily due to expenses related to the acquisition of the Madison facility.

Government Regulation

Governmental authorities in the U.S. and other countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of drugs and biologic products. All of our foreseeable product candidates are expected to be regulated as drug products.

In the U.S., the FDA regulates drug products under the Federal Food, Drug and Cosmetic Act (the FDCA), and other laws within the Public Health Service Act. Failure to comply with applicable U.S. requirements, both before and after approval, may lead to administrative and judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecutions. Before drug products are marketed they must be approved by the FDA. The steps required before a novel drug product is approved by the FDA include: (1) pre-clinical laboratory, animal, and formulation tests; (2) submission to the FDA of an Investigational New Drug Application (IND) for human clinical testing, which must become effective before human clinical trials may begin; (3) adequate and well-controlled clinical trials to establish the safety and effectiveness of the product for each indication for which approval is sought; (4) submission to the FDA of a New Drug Application (NDA); (5) satisfactory completion of a FDA inspection of the manufacturing facility or facilities at which the drug product is produced to assess compliance with cGMP; and FDA review and finally (6) approval of an NDA.

Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions, such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. There can be no assurance that submission of an IND will result in FDA authorization to commence clinical trials. Once an IND is in effect, each clinical trial to be conducted under the IND must be submitted to the FDA, which may or may not allow the trial to proceed.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified physician-investigators and healthcare personnel. Clinical trials are typically conducted in three defined phases, but the phases may overlap or be combined. Phase 1 usually involves the initial administration of the investigational drug or biologic product to healthy individuals to evaluate its safety, dosage tolerance and pharmacodynamics. Phase 2 usually involves trials in a limited patient population, with the disease or condition for which the test material is being developed, to evaluate dosage tolerance and appropriate dosage; identify possible adverse side effects and safety risks; and preliminarily evaluate the effectiveness of the drug or biologic for specific indications. Phase 3 trials usually further evaluate effectiveness and test further for safety by administering the drug or biologic candidate in its final form in an expanded patient population. Our product development partners, the FDA, or we may suspend clinical trials at any time on various grounds, including any situation where we believe that patients are being exposed to an unacceptable health risk or are obtaining no medical benefit from the test material.

Assuming successful completion of the required clinical testing, the results of the pre-clinical trials and the clinical trials, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. Before approving an application, the FDA will usually inspect the facilities where the product is manufactured, and will not approve the product unless cGMP compliance is satisfactory. If the FDA determines the NDA is not acceptable, the FDA may outline the deficiencies in the NDA and often will request additional information. If the FDA approves the NDA, certain changes to the approved product, such as adding new indications, manufacturing changes or additional labeling claims are subject to further FDA review and approval. The testing and approval process requires substantial time, effort and financial resources, and approval on a timely basis, if at all, cannot be guaranteed.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other application to market the same drug for the same indication, except in very limited circumstances, for seven years.

In addition, regardless of the type of approval, we and our partners are required to comply with a number of FDA requirements both before and after approval. For example, drug makers are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotion for our products. In addition, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in all areas of regulatory compliance, including production and quality control to comply with cGMP. In addition, discovery of problems, such as safety problems, may result in changes in labeling or restrictions on a product manufacturer or NDA holder, including removal of the product from the market.

Corporate Information

Unless otherwise noted, (1) the term Arrowhead refers to Arrowhead Research Corporation, a Delaware corporation, (2) the terms the Company, we, us, and our, refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term Subsidiaries refers collectively to Arrowhead Madison Inc. (Madison , formerly known as Roche Madison, Inc.), Alvos Therapeutics, Inc. (Alvos), Calando Pharmaceuticals, Inc. (Calando), Ablaris Therapeutics, Inc. (Ablaris), Agonn Systems, Inc. (Agonn ,) and Tego Biosciences Corporation (Tego) as well as our former subsidiary, Unidym, Inc. (Unidym), which was divested in January 2011, (4) the term Minority Investments refers collectively to Nanotope, Inc. (Nanotope) and Leonardo Biosystems, Inc. (Leonardo) in which the company holds a less than majority ownership position, and (5) the term Common Stock refers to Arrowhead s Common Stock and the term stockholder(s) refers to the holders of Arrowhead Common Stock.

Arrowhead was originally incorporated in South Dakota in 1989, and was reincorporated in Delaware in 2000. The Company s principal executive offices are located at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, and its telephone number is (626) 304-3400. We operate a 24,000 square foot research and development facility in Madison, Wisconsin. As of September 30, 2012, Arrowhead had 52 full-time employees.

Other Business Interests

Leonardo Biosystems, Inc.

Leonardo is a drug delivery company that employs a novel multi-stage drug delivery mechanism aimed at dramatically increasing targeting efficiency of pharmaceuticals. Arrowhead has an approximately 3% ownership interest in Leonardo. Leonardo s silicon micro-particulate technology involves transporting a therapeutic agent past multiple biological barriers using multiple carriers, each optimized for a specific barrier. Leonardo s proprietary primary vehicles are designed to preferentially accumulate at tumor vasculature. Secondary carriers are then released from the primary carriers that are designed to accumulate around tumor cells and release their therapeutic payloads. Pre-clinical testing in animal disease models suggests that Leonardo s platform enables significantly increased targeting of tumors and also provides sustained release of cancer therapies. Further development of Leonardo s technology is dependent on cash resources available to Leonardo.

Nanotope, Inc.

Nanotope is a regenerative medicine company with license to a suite of nanotechnology-based products customized to regenerate specific tissues: including neuronal, bone and cartilaginous tissues. During 2012, Nanotope closed its R&D facility and ceased internal development of its technology. Development is continuing at Northwestern University in the lab of Sam Stupp, Nanotope s scientific founder. Arrowhead has an approximately 23% ownership interest in Nanotope.

Unidym, Inc.

In January 2011, Arrowhead sold Unidym, Inc. to Wisepower Co., Ltd., a publicly-traded, Seoul, Korea-based electronics company (KOSDAQ: 040670). Unidym was a majority-owned subsidiary that developed nanotechnology-enabled materials to be used in the manufacturing of certain electronics components. Upfront consideration consisted of stock and convertible bonds valued at $5,000,000 with certain restrictions as to timing of stock sales. Additional cash earn-out payments of up to US $140 million are possible based on cumulative sales and licensing milestones, and up to 40% of licensing revenue.

ITEM 1A. RISK FACTORS

You should carefully consider the risks discussed below and all of the other information contained in this report in evaluating us and an investment in our securities. If any of the following risks and uncertainties should occur, they could have a material adverse effect on our business, financial condition or results of operations. In that case, the trading price of our Common Stock could decline. Additionally, we note that we are a development stage company and we have accrued net losses annually since inception. We urge you to consider our likelihood of success and prospects in light of the risks, expenses and difficulties frequently encountered by entities at similar stages of development.

Risks Related to Our Financial Condition

Our independent auditors have issued a report questioning our ability to continue as a going concern.

The report of our independent auditors contained in our financial statements explains that we have not yet established an ongoing source of revenue sufficient to cover operating costs and allow us to continue as a going concern. Our ability to continue as a going concern is dependent on obtaining adequate capital to fund operating losses until we become profitable. If we are unable to obtain adequate capital, we may have to delay, scale back, or discontinue the development and/or commercialization of one or more product candidates, or relinquish or otherwise dispose of rights to technologies, product candidates, or products that we would otherwise seek to develop or commercialize ourselves and/or cease operations.

We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.

We have incurred net losses since our inception, including net losses of $22.1 million for the year ended September 30, 2012 and a cumulative net loss since inception of approximately $153.7 million. We expect that our operating losses will continue as we fund our drug development and discovery efforts. To achieve profitability, we must, either directly or through licensing and/or partnering relationships, successfully develop and obtain regulatory approval for a drug candidate and effectively manufacture, market and sell any drugs we successfully develop. Even if we successfully commercialize drug candidates that receive regulatory approval, we may not be able to realize revenues at a level that would allow us to achieve or sustain profitability. Accordingly, we may never generate significant revenue and, even if we do generate significant revenue, we may never achieve profitability.

We have limited cash resources.

Our business currently does not generate the cash that is necessary to finance our operations. We incurred net losses of approximately $22.1 million in 2012 and $153.7 million since our inception. Subject to the success of the research and development programs of our company and our partners, and potential licensing or partnering transactions, we will need to raise significant additional capital in the immediate future to:

- Fund research and development activities relating to our development of our product candidates, including clinical and pre-clinical trials;
- Fund our general and administrative activities;
- Pursue licensing opportunities for our technologies;
- Protect our intellectual property; and
- Retain our management and technical staff.

Our future capital needs depend on many factors, including:

- The scope, duration and expenditures associated with our research and development;
- Continued scientific progress in these programs;
- The outcome of potential partnering or licensing transactions, if any;
- Competing technological developments;
- Our proprietary patent position, if any, in our products; and
- The regulatory approval process for our products.

We will need to raise substantial additional funds through public or private equity offerings, debt financings or additional strategic alliances and licensing arrangements in the immediate future to continue our operations. We may not be able to obtain additional financing on terms favorable to us, if at all. General market conditions, as well as market conditions for companies that are facing financial distress, may make it very difficult

for us to seek financing from the capital markets, and the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our stockholders will result, which may substantially dilute the value of your investment. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants that could limit our flexibility in conducting future business activities and, in the event of insolvency, would be paid before holders of equity securities received any distribution of corporate assets. We may be required to relinquish rights to our technologies or drug candidates, or grant licenses on terms that are not favorable to us, in order to raise additional funds through alliance, joint venture or licensing arrangements. If adequate funds are not available, we may have to further delay, reduce or eliminate one or more of our planned activities. These actions would likely reduce the market price of our common stock.

The current financial market conditions may exacerbate certain risks affecting our business.

We do not yet generate substantial revenue, and our operations and research and development activities have been primarily funded to date through the sale of Company securities and securities of our Subsidiaries. The global financial markets are volatile and those market conditions may impair our ability to raise the capital we require. If we are unable to secure additional cash resources from the sale of securities or other sources, it could become necessary to slow or suspend development efforts. In addition, we may have to reduce expenses, which could impair our ability to manage our business. Even if investment capital is available to us, the terms may be onerous.

Because we have not generated significant revenues to cover our operating expenses, we are dependent on raising additional capital from investors or lenders.

To date, we have only generated a small amount of revenue. Given our strategy of financing new and unproven technology research, there can be no assurance we will ever generate significant revenue. Our revenue-producing opportunities depend on our ability to attract collaborations or out-licenses with other companies, receive milestone and royalty payments from prior divestitures, and/or generate income from the sales of products. These sources of revenue are uncertain as to the amount and timing of potential revenue. Accordingly, our revenue prospects are uncertain and we must plan to finance our operations through the sales of equity securities or debt financing. If we are unable to continue raising operating capital from these sources, we may be forced to curtail or cease our operations.

We will need to achieve commercial acceptance of our applications to generate revenues and achieve profitability.

Even if our research and development efforts yield technologically feasible applications, we may not successfully develop commercial products which would take years to study in human clinical trials prior to regulatory approval, and, even if successfully developed, we may not do so on a timely basis. During this development period, superior competitive technologies may be introduced which could diminish or extinguish the potential commercial uses for our drug candidates. Additionally, the degree to which patients and consumers will adopt any product we develop is uncertain. We cannot predict whether significant commercial market acceptance for our products, if approved, will ever develop, and we cannot reliably estimate the projected size of any such potential market. Our revenue growth and achievement of profitability will depend substantially on our ability to introduce new technological applications to manufacturers for products accepted by customers. If we are unable to cost-effectively achieve acceptance of our technology among the medical establishment and patients, or if the associated products do not achieve wide market acceptance, our business will be materially and adversely affected.

We have debt on our consolidated balance sheet through our subsidiary, Calando, which could have negative consequences if we were unable to repay the principal or interest due.

Calando has a $500,000 unsecured convertible promissory note outstanding. The note bears 10% interest accrued annually, and matures in November 2013. The note is payable at two times face value at maturity and upon the occurrence of certain events, including, the license of Calando s siRNA delivery system. If Calando is unable to meet its obligations to the bearer of the note, Arrowhead may not be in a position to lend Calando sufficient cash to pay such demand note. Unless other sources of financing become available, this could result in Calando s insolvency.

Our Subsidiaries are party to technology license agreements with third parties that require us to satisfy obligations to keep them effective and, if these agreements are terminated, our technology and our business would be seriously and adversely affected.

Through our Subsidiaries, we are party into exclusive, long-term license agreements with University of Texas MD Anderson Cancer Center, California Institute of Technology, Alnylam Pharmaceuticals, Inc. and other entities to incorporate their proprietary technologies into our proposed products. These license agreements require us to pay royalties and satisfy other conditions, including conditions in some cases related to the commercialization of the licensed technology. We may not be able to successfully incorporate these technologies into marketable products or, if we do, whether sales will be sufficient to recover the amounts that we are obligated to pay to the licensors. If we fail to satisfy our obligations under these agreements the terms of the licenses may be materially modified, such as by rendering the licenses non-exclusive, or may give our licensors the right to terminate their respective agreement with us, which would limit our ability to implement our current business plan and harm our business and financial condition.

Risks Related to Our Company

Drug development is time consuming, expensive and risky.

We are focused on technology related to new and improved pharmaceutical candidates. Product candidates that appear promising in the early phases of development, such as in animal and early human clinical trials, often fail to reach the market for a number of reasons, such as:

- Clinical trial results may be unacceptable, even though preclinical trial results were promising;
- Inefficacy and/or harmful side effects in humans or animals;
- The necessary regulatory bodies, such as the U.S. Food and Drug Administration, may not approve our potential product for the intended use; and
- Manufacturing and distribution may be uneconomical.

For example, the positive pre-clinical results for Adipotide in animals may not be replicated in human clinical studies or it may be found to be unsafe in humans. Additionally, clinical trial results are frequently susceptible to varying interpretations by scientists, medical personnel, regulatory personnel, statisticians and others, which often delays, limits, or prevents further clinical development or regulatory approvals of potential products. Clinical trials can take many years to complete, including the process of study design, clinical site selection and the

enrollment of patients. As a result, we can experience significant delays in completing clinical studies, which can increase the cost of developing a drug candidate. If our drug candidates are not successful in human clinical trials, we may be forced to curtail or abandon certain development programs. If we experience significant delays in commencing or completing our clinical studies, we could suffer from significant cost overruns, which could negatively affect our capital resources and our ability to complete these studies.

We may be unable to attract revenue-generating collaborations with other pharmaceutical and biotech companies to advance our drug candidates.

Our business strategy includes obtaining collaborations with other pharmaceutical and biotech companies to support the development of our therapeutic siRNA and other drug candidates. We may not be able to attract such partners, and even if we are able to enter into such partnerships, the terms may be less favorable than anticipated. Further, entering into partnership agreements may limit our commercialization options and/or require us to share revenues and profits with our partners.

Our products are in the early stages of our development and because we have a short development history with both DPCs and Homing Peptides, there is a limited amount of information about us upon which you can evaluate our business and prospects.

We have not begun to market or generate revenues from the commercialization of any products. We have only a limited history upon which one can evaluate our targeted therapeutic business and prospects as our therapeutic products are still at an early stage of development. Thus, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

Execute product development activities using an unproven technology;

Build, maintain and protect a strong intellectual property portfolio;

Gain acceptance for the development and commercialization of any product we develop;

Develop and maintain successful strategic relationships; and

Manage our spending and cash requirements as our expenses are expected to increase in the near term due to preclinical and clinical trials.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop products, raise capital, expand our business or continue our operations.

We may lose a considerable amount of control over our intellectual property and may not receive anticipated revenues in strategic transactions, particularly where the consideration is contingent on the achievement of development or sales milestones.

Our business model has been to develop new technologies and to exploit the intellectual property created through the research and development process to develop commercially successful products. Calando has licensed a portion of its technology to Cerulean Pharma, Inc. and we intend to pursue licensing arrangements with other companies. A significant portion of the potential value from these licenses is tied to the achievement of the development and sales milestones, which we cannot control. Similarly, the majority of the consideration, up to $140 million, potentially payable by Wisepower in connection with our sale of Unidym is tied to the achievement of commercialization milestones, which we cannot control. Although Wisepower and Cerulean are required to use certain minimum efforts to achieve the post-closing milestones, we cannot control whether they actually achieve these milestones. If the acquirers fail to achieve performance milestones, we may not receive a significant portion of the total value of any sale, license or other strategic transaction.

There are substantial risks inherent in attempting to commercialize new technological applications, and, as a result, we may not be able to successfully develop products for commercial use.

Our research and development efforts involve therapeutics based on nanotechnology and RNA interference, which are largely unproven technologies. Our scientists and engineers are working on developing technology in various stages. However, such technology s commercial feasibility and acceptance are unknown. Scientific research and development requires significant amounts of capital and takes a long time to reach commercial viability, if at all. To date, our research and development projects have not produced commercially viable applications, and may never do so. During the research and development process, we may experience technological barriers that we may be unable to overcome. Because of these uncertainties, it is possible that none of our potential applications will be successfully developed. If we are unable to

successfully develop applications of our technology for commercial use, we will be unable to generate revenue or build a sustainable or profitable business.

We will need to establish additional relationships with strategic and development partners to fully develop and market our products.

We do not possess all of the financial and development resources necessary to develop and commercialize products that may result from our technologies on a mass scale. Unless we expand our product development capacity and enhance our internal marketing capability, we will need to make appropriate arrangements with strategic partners to develop and commercialize current and future products. If we do not find appropriate partners, or if our existing arrangements or future agreements are not successful, our ability to develop and commercialize products could be adversely affected. Even if we are able to find collaborative partners, the overall success of the development and commercialization of product candidates in those programs will depend largely on the efforts of other parties and is beyond our control. In addition, in the event we pursue our commercialization strategy through collaboration, there are a variety of technical, business and legal risks, including:

A development partner would likely gain access to our proprietary information, potentially enabling the partner to develop products without us or design around our intellectual property;

We may not be able to control the amount and timing of resources that our collaborators may be willing or able to devote to the development or commercialization of our product candidates or to their marketing and distribution; and

Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts our management s resources.

The occurrence of any of the above events or other related events not foreseen by us could impair our ability to generate revenues and harm our business and financial condition.

We may not be able to effectively secure first-tier technologies when competing against other investors.

Our success may require that we acquire new or complimentary technologies. However, we compete with a substantial number of other companies that may also compete for technologies we desire. In addition, many venture capital firms and other institutional investors, as well as other pharmaceutical and biotech companies, invest in companies seeking to commercialize various types of emerging technologies. Many of these companies have greater financial, scientific and commercial resources than us. Therefore, we may not be able to secure the technologies we desire. Furthermore, should any commercial undertaking by us prove to be successful, there can be no assurance competitors with greater financial resources will not offer competitive products and/or technologies.

We rely on outside sources for various components and processes for our products.

We rely on third parties for various components and processes for our products. While we try to have at least two sources for each component and process, we may not be able to achieve multiple sourcing because there may be no acceptable second source, other companies may choose not to work with us, or the component or process sought may be so new that a second source does not exist, or does not exist on acceptable terms. There may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators which is beyond our control. If such third parties are unable to satisfy their commitments to us, our business would be adversely affected. Therefore, it is possible that our business plans will have to be slowed down or stopped completely at times due to our inability to obtain required raw materials, components and outsourced processes at an acceptable cost, if at all, or to get a timely response from vendors.

We must overcome the many obstacles associated with integrating and operating varying development programs.

Our model to integrate and oversee research and development projects presents many risks, including:

The difficulty of integrating operations and personnel; and

The diversion of our management s attention as a result of evaluating, negotiating and integrating acquisitions or new business ventures.

If we are unable to timely and efficiently design and integrate administrative and operational support for our Subsidiaries, we may be unable to manage projects effectively, which could adversely affect our ability to meet our business objectives and the value of an investment in the Company could decline.

In addition, consummating acquisitions and strategic relationships could adversely impact our cash position, and dilute stockholder interests, for many reasons, including:

Collaboration terms that decrease future cash flows from products in exchange for near term benefits;

Changes to our income to reflect the amortization of acquired intangible assets, including goodwill;

Interest costs and debt service requirements for any debt incurred to fund our growth strategy; and

Any issuance of securities to fund our operations or growth, which dilutes or lessens the rights of current stockholders.

Our success depends on the attraction and retention of senior management and scientists with relevant expertise.

Our future success depends to a significant extent on the continued services of our key employees, including Dr. Anzalone, our President and Chief Executive Officer, Dr. Bruce Given, our Chief Operating Officer, and Ken Myszkowski, our Chief Financial Officer. We do not maintain key man life insurance for any of our executives. Our ability to execute our strategy also will depend on our ability to continue to attract and retain qualified scientists and management. If we are unable to find, hire and retain qualified individuals, we could have difficulty implementing our business plan in a timely manner, or at all.

Members of our senior management team and Board may have a conflict of interest in also serving as officers and/or directors of our Subsidiaries.

While we expect that our officers and directors who also serve as officers and/or directors of our Subsidiaries will comply with their fiduciary duties owed to our stockholders, they may have conflicting fiduciary obligations to our stockholders and the minority stockholders of our Subsidiaries. Specifically, Dr. Anzalone, our President and CEO, is the founder, CEO and a board member of Nanotope, a regenerative medicine company in which the Company owns a 23% interest. Further, Dr. Anzalone as well as Dr. Mauro Ferrari, an Arrowhead board member, are board members of Leonardo, a drug delivery company in which Arrowhead owns a 3% interest. Dr. Anzalone owns a noncontrolling interest in the stock of Nanotope. Drs. Anzalone and Ferrari own a noncontrolling interest in Leonardo. Douglass Given, a member of our board of directors, is the brother of Bruce Given. To the extent that any of our directors choose to recuse themselves from particular Board actions to avoid a conflict of interest, the other members of our Board of Directors will have a greater influence on such decisions.

We face uncertainty related to healthcare reform, pricing and reimbursement, which could reduce our revenue.

In the United States, President Obama signed in March 2010 the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, PPACA), which is expected to substantially change the way health care is financed by both governmental and private payers. PPACA provides for changes to extend medical benefits to those who currently lack insurance coverage, encourages improvements in the quality of health care items and services, and significantly impacts the U.S. pharmaceutical industry in a number of ways, further listed below. By extending coverage to a larger population, PPACA may substantially change the structure of the health insurance system and the methodology for reimbursing medical services, drugs and devices. These structural changes, as well as other changes that may be made as part of deficit and debt reduction efforts in Congress, could entail modifications to the existing system of private payers and government programs, such as Medicare, Medicaid and State Children s Health Insurance Program, as well as the creation of a government-sponsored healthcare insurance source, or some combination of both. Such restructuring of the coverage of medical care in the United States could impact the extent of reimbursement for prescribed drugs, including our product candidates, biopharmaceuticals, and medical devices. Some of the specific PPACA provisions, among other things:

- Establish annual, non-deductible fees on any entity that manufactures or imports certain branded prescription drugs and biologics, beginning in 2011;
- Increase minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program;
- Extend manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- Establish a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research;
- Require manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D, beginning in 2011; and
- Increase the number of entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective January 2010.

If future reimbursement for approved product candidates, if any, is substantially less than we project, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.

Sales of any approved drug candidate will depend in part on the availability of coverage and reimbursement from third-party payers such as government insurance programs, including Medicare and Medicaid, private health insurers, health maintenance organizations and other health care related organizations. Accordingly, coverage and reimbursement may be uncertain. Adoption of any drug candidate by the medical community may be limited if third-party payers will not offer coverage. Cost control initiatives may decrease coverage and payment levels for

any new drug and, in turn, the price that we will be able to charge. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payers. Any denial of private or government payer coverage or inadequate reimbursement could harm our business and reduce our revenue.

In addition, both the federal and state governments in the United States and foreign governments continue to propose and pass new legislation affecting coverage and reimbursement policies, which are designed to contain or reduce the cost of health care, as well as hold public hearings on these matters, which has resulted in certain private companies dropping the prices of their drugs. Further federal and state proposals and healthcare reforms are likely, which could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. There may be future changes that result in reductions in current coverage and reimbursement levels for our product candidates, if approved and commercialized, and we cannot predict the scope of any future changes or the impact that those changes would have on our operations.

There may be a difference in the investment valuations that we used when making initial and subsequent investments in our Subsidiaries and minority investments and actual market values.

Our investments in our Subsidiaries and noncontrolling interests were the result of negotiation with subsidiary management and equity holders, and the investment valuations may not always have been independently verified. Traditional methods used by independent valuation analysts include a discounted cash flow analysis and a comparable company analysis. We have not generated a positive cash flow to date and do not expect to generate significant cash flow in the near future. Additionally, we believe that few comparable public companies exist to provide meaningful valuation comparisons. Accordingly, we have not always sought independent valuation analysis in connection with our investments and may have invested in our various holdings at higher or lower valuations than an independent source would have recommended. There may be no correlation between the investment valuations that we used over the years for our investments and the actual market values. If we should eventually sell all or a part of any of our consolidated business or that of a subsidiary, the ultimate sale price may be for a value substantially different than previously determined by us, which could materially and adversely impair the value of our Common Stock.

Risks Related to Our Intellectual Property

Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.

We have licensed rights to pending patents and have filed and expect to continue to file patent applications. Researchers sponsored by us may also file patent applications that we choose to license. If a particular patent is not granted, the value of the invention described in the patent would be diminished. Further, even if these patents are granted, they may be difficult to enforce. Even if successful, efforts to enforce our patent rights could be expensive, distracting for management, cause our patents to be invalidated, and frustrate commercialization of products. Additionally, even if patents are issued and are enforceable, others may independently develop similar, superior or parallel technologies to any technology developed by us, or our technology may prove to infringe upon patents or rights owned by others. Finally, patent prosecution is expensive, and we may be forced to curtail prosecution if our cash resources are limited. Thus, the patents held by or licensed to us may not afford us any meaningful competitive advantage. If we are unable to derive value from our licensed or owned intellectual property, the value of your investment may decline.

We may be subject to patent infringement claims, which could result in substantial costs and liability and prevent us from commercializing our potential products.

Because the intellectual property landscape in the fields in which we participate is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate without infringing on third party rights. However, we are currently aware of certain patent rights held by third parties that, if found to be valid and enforceable, could be alleged to render one or more of our business lines infringing. If a claim should be brought and is successful, we may be required to pay substantial damages, be forced to abandon any affected business lines and/or seek a license from the patent holder. In addition, any patent infringement claims brought against us, whether or not successful, may cause us to incur significant expenses and divert the attention of our management and key personnel from other business concerns. These could negatively affect our results of operations and prospects. We cannot be certain that patents owned or licensed by us or our Subsidiaries will not be challenged by others.

In addition, if our potential products infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our customers, and we may be required to indemnify our customers for any damages they suffer as a result of these claims. The claims may require us to initiate or defend protracted and costly litigation on behalf of customers, regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of our customers or may be required to obtain licenses for the products they use. If we cannot obtain all necessary licenses on commercially reasonable terms, we may be unable to continue selling such products.

Our technology licensed from various third parties may be subject to government rights and retained rights of the originating research institutions.

We license technology from the University of Texas MD Anderson Cancer Center, Caltech, and other universities and companies. Our licensors may have obligations to government agencies or universities. Under their agreements, a government agency or university may obtain certain rights over the technology that we have developed and licensed, including the right to require that a compulsory license be granted to one or more third parties selected by the government agency.

In addition, our licensors often retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

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Risks Related to Regulation of Our Products

Our corporate compliance program cannot guarantee that we are in compliance with all applicable federal and state regulations.

Our operations, including our research and development and our commercialization efforts, such as clinical trials, manufacturing and distribution, are subject to extensive federal and state regulation. While we have developed and instituted a corporate compliance program, we cannot be assured that the Company or our employees are, or will be in compliance with all potentially applicable federal and state regulations or laws. If we fail to comply with any of these regulations or laws, a range of actions could result, including, but not limited to, the termination of clinical trials, the failure to approve a commercialized product, significant fines, sanctions, or litigation, any of which could harm our business and financial condition.

Risks Related to our Stock

Stockholder equity interest may be substantially diluted in any additional financing.

Our certificate of incorporation authorizes the issuance of 145,000,000 shares of Common Stock and 5,000,000 shares of Preferred Stock, on such terms and at such prices as our Board of Directors may determine. Adjusted for the 1 for 10 stock split that was implemented on November 17, 2011, as of September 30, 2012, we had 13,579,185 shares of Common Stock issued and outstanding. The issuance of additional securities in financing transactions by us or through the exercise of options or warrants will dilute the equity interests of our existing stockholders, perhaps substantially, and might result in dilution in the tangible net book value of a share of our Common Stock, depending upon the price and other terms on which the additional shares are issued.

Our Common Stock price has fluctuated significantly over the last several years and may continue to do so in the future, without regard to our results of operations and prospects.

Because we are a development stage company, there are few objective metrics by which our progress may be measured. Consequently, we expect that the market price of our Common Stock will likely continue to fluctuate significantly. We may not generate substantial revenue from the license or sale of our technology for several years, if at all. In the absence of product revenue as a measure of our operating performance, we anticipate that investors and market analysts will assess our performance by considering factors such as:

Announcements of developments related to our business;

Our ability to enter into or extend investigation phase, development phase, commercialization phase and other agreements with new and/or existing partners;

Announcements regarding the status of any or all of our collaborations or products;

Market perception and/or investor sentiment regarding our technology;

Announcements regarding developments in the RNA interference or biotechnology fields in general;

Market perception and/or announcements regarding other companies developing products in the field of RNA interference;

The issuance of competitive patents or disallowance or loss of our patent rights; and

Variations in our operating results.

We will not have control over many of these factors but expect that they may influence our stock price. As a result, our stock price may be volatile and such volatility could result in the loss of all or part of your investment. Additionally, in the past, when the market price of a stock has been volatile, holders of that stock have often initiated securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

The market for purchases and sales of our Common Stock may be very limited, and the sale of a limited number of shares could cause the price to fall sharply.

Although our Common Stock is listed for trading on the NASDAQ Capital Market, historically our securities have been relatively thinly traded. Investor trading patterns could serve to exacerbate the volatility of the price of the stock. For example, mandatory sales of our Common Stock by institutional holders could be triggered if an investment in our Common Stock no longer satisfies their investment standards and guidelines. Accordingly, it may be difficult to sell shares of our Common Stock quickly without significantly depressing the value of the stock. Unless we are successful in developing continued investor interest in our stock, sales of our stock could continue to result in major fluctuations in the price of the stock.

If securities or industry analysts do not publish research reports about our business or if they make adverse recommendations regarding an investment in our stock, our stock price and trading volume may decline.

The trading market for our Common Stock can be influenced by the research and reports that industry or securities analysts publish about our business. We do not currently have and may never obtain research coverage by industry or securities analysts. Investors have many investment opportunities and may limit their investments to companies that receive coverage from analysts. If no industry or securities analysts commence coverage of the Company, the trading price of our stock could be negatively impacted. In the event we obtain industry or security analyst coverage, if one or more of the analysts downgrade our stock or comment negatively on our prospects, our stock price may decline. If one or more of these analysts cease to cover our industry or us or fails to publish reports about the Company regularly, our Common Stock could lose visibility in the financial markets, which could also cause our stock price or trading volume to decline.

The market price of our Common Stock may be adversely affected by the sale of shares by our management or founding stockholders.

Sales of our Common Stock by our officers, directors and founding stockholders could adversely and unpredictably affect the price of those securities. Additionally, the price of our Common Stock could be affected even by the potential for sales by these persons. We cannot predict the effect that any future sales of our Common Stock, or the potential for those sales, will have on our share price. Furthermore, due to relatively low trading volume of our stock, should one or more large stockholders seek to sell a significant portion of their stock in a short period of time, the price of our stock may decline.

We do not intend to declare cash dividends on our Common Stock.

We will not distribute cash to our stockholders unless and until we can develop sufficient funds from operations to meet our ongoing needs and implement our business plan. The time frame for that is unpredictable and investors should not expect dividends in the near future, if at all.

Our Board of Directors has the authority to issue shares of blank check preferred stock, which may make an acquisition of the Company by another company more difficult.

We have adopted and may in the future adopt certain measures that may have the effect of delaying, deferring or preventing a takeover or other change in control of the Company that a holder of our Common Stock might consider in its best interest. Specifically, our Board of Directors, without further action by our stockholders, currently has the authority to issue up to 5,000,000 shares of preferred stock and to fix the rights (including voting rights), preferences and privileges of these shares (blank check preferred). Such preferred stock may have rights, including economic rights, senior to our Common Stock.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

At September 30, 2012, we had leases for our corporate headquarters, located in Pasadena, California, and our research facility in Madison, Wisconsin. The Company does not own any real property. The following table summarizes the company s leased facilities:

	Office Space	Monthly Rent	Lease Commencement	Lease Term
Pasadena, CA	5,300 sq. ft.	$ 13,000	August 16, 2011	5.5 years
Madison, WI	24,000 sq. ft.	$ 56,500	February 16, 2009	10 Years

ITEM 3. LEGAL PROCEEDINGS

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Price Range of Common Stock

Our Common Stock is traded on the NASDAQ Stock Market under the symbol ARWR . The following table sets forth the high and low sales prices for a share of the Company s Common Stock during each period indicated. On November 17, 2011, the Company effected a 1 for 10 reverse stock split. The share prices in the table below are shown on a post-split basis.

	Fiscal Year Ended September 30,			
	2012		2011	
	High	Low	High	Low
1st Quarter	$ 7.50	$ 3.60	$ 11.00	$ 8.30
2nd Quarter	6.38	4.13	10.00	6.00
3rd Quarter	7.14	3.12	7.00	4.30
4th Quarter	3.84	2.60	5.90	3.70

Shares Outstanding

At December 19, 2012, an aggregate of 15,719,079 shares of the Company s Common Stock were issued and outstanding, and were owned by 293 stockholders of record, based on information provided by the Company s transfer agent.

Dividends

The Company has never paid dividends on its Common Stock and does not anticipate that it will do so in the foreseeable future.

Securities Authorized for Issuance Under the Equity Compensation Plans

The disclosure required under this item related to equity compensation plans is incorporated by reference from Item 12, under the caption Equity Compensation Plan Information in this Annual Report on Form 10-K.

Sales of Unregistered Securities

All information under this Item has been previously reported on our Current Reports on Form 8-K.

Repurchases of Equity Securities

We did not repurchase any shares of our Common Stock during fiscal 2012 or fiscal 2011.

ITEM 6. SELECTED FINANCIAL DATA

As a Smaller Reporting Company, we are not required to provide this information.

ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Description of Business

Unless otherwise noted, (1) the term Arrowhead refers to Arrowhead Research Corporation, a Delaware corporation, (2) the terms the Company, we, us, and our, refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term Subsidiaries refers collectively to Arrowhead Madison Inc. (Madison), formerly

known as Roche Madison, Inc. , Alvos Therapeutics, Inc. (Alvos), Calando Pharmaceuticals, Inc. (Calando), Ablaris Therapeutics, Inc. (Ablaris), Agonn Systems, Inc. (Agonn), and Tego Biosciences Corporation (Tego) as well as our former subsidiary, Unidym, Inc. (Unidym), which was divested in January 2011, (4) the term Minority Investments refers collectively to Nanotope, Inc. (Nanotope) and Leonardo Biosystems, Inc. (Leonardo) in which the company holds a less than majority ownership position, and (5) the term Common Stock refers to Arrowhead s Common Stock and the term stockholder(s) refers to the holders of Arrowhead Common Stock. All Arrowhead share and per share data have been adjusted to reflect a one for ten reverse stock split effected on November 17, 2011.

Overview

Arrowhead Research Corporation is a clinical stage targeted therapeutics company with development programs in oncology, obesity, and chronic hepatitis B virus infection. Arrowhead is focused on creating new therapeutics that are preferentially taken up by target tissues in order to maximize a drug s efficacy and potentially limit side effects associated with exposure to healthy cells. Arrowhead has assembled a broad set of technologies and licenses to enable targeted RNAi therapeutics capable of silencing specific gene products in specific cells. Arrowhead has also assembled a proprietary targeting library that may be used with its RNAi platforms as well as with small molecule or peptide drugs. These platforms have yielded several drug candidates under both internal and partnered development.

Critical Accounting Policies and Estimates

Management makes certain judgments and uses certain estimates and assumptions when applying accounting principles generally accepted in the United States in the preparation of our Consolidated Financial Statements. We evaluate our estimates and judgments on an ongoing basis and base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances. Our experience and assumptions form the basis for our judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may vary from what we anticipate and different assumptions or estimates about the future could change our reported results. We believe the following accounting policies are the most critical to us, in that they are important to the portrayal of our consolidated financial statements and require our most difficult, subjective or complex judgments in the preparation of our consolidated financial statements. For further information, see *Note 1, Organization and Significant Accounting Policies*, to our Consolidated Financial Statements which outlines our application of significant accounting policies and new accounting standards.

Revenue Recognition

Revenue from product sales are recorded when persuasive evidence of an arrangement exists, title has passed and delivery has occurred, a price is fixed and determinable, and collection is reasonably assured.

We may generate revenue from technology licenses, collaborative research and development arrangements, research grants and product sales. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable and/or guaranteed technology license fees, collaborative research funding, and various milestone and future product royalty or profit-sharing payments.

Revenue associated with research and development funding payments under collaborative agreements is recognized ratably over the relevant periods specified in the agreement, generally the research and development period. Revenue from up-front license fees, milestones and product royalties are recognized as earned based on the completion of the milestones and product sales, as defined in the respective agreements. Payments received in advance of recognition as revenue are recorded as deferred revenue.

Business Combinations

In October 2011, we acquired all of the outstanding common stock of Roche Madison, Inc. and certain related intellectual property assets for a $50,000 promissory note and 1,288,158 shares of Arrowhead Common Stock, an estimated consideration value of $5.1 million on the date of the acquisition. We assigned the value of the consideration to the tangible assets and identifiable intangible assets and the liabilities assumed on the basis of their fair values on the date of acquisition. The excess of net assets over the consideration was recorded as a nonoperating gain.

In April 2012, we acquired all of the outstanding common stock of Alvos Therapeutics, Inc. in exchange for the issuance of 315,457 shares of Arrowhead Common Stock, valued at $2.0 million at the time of acquisition. The consideration was assigned to its tangible and intangible assets, and liabilities based on estimated fair values at the time of acquisition.

The allocation of value to certain items, including property and equipment, intangible assets and certain liabilities require management judgment, and is based upon the information available at the time of acquisition.

Impairment of Long-lived Assets

We review long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of assets may not be fully recoverable or that our assumptions about the useful lives of these assets are no longer appropriate. If impairment is indicated, recoverability is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset exceeds the fair value of the asset.

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Impairment of Intangible assets

Intangible assets consist of in-process research and development, patents and license agreements acquired in conjunction with a business acquisition. Intangible assets are monitored for potential impairment whenever events or circumstances indicate that the carrying amount may not be recoverable, and are also reviewed annually to determine whether any impairment is necessary. Based on early adoption of ASU 2012-02, the annual review of intangible assets is performed via a two-step process. First, a qualitative assessment is performed to determine if it is more likely than not that the intangible asset is impaired. If required, a quantitative assessment is performed and, if necessary, impairment is recorded.

Stock-Based Compensation

We recognize stock-based compensation expense based on the grant date fair value using the Black-Scholes options pricing model, which requires us to make assumptions regarding certain variables including the risk-free interest rate, expected stock price volatility, and the expected life of the award. The assumptions used in calculating stock-based compensation expense represent management s best estimates, but these estimates involve inherent uncertainties, and if factors change or the Company used different assumptions, its stock-based compensation expense could be materially different in the future.

Derivative Assets and Liabilities

We account for warrants and other derivative financial instruments as either equity or assets/liabilities based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded as additional paid-in capital on our consolidated balance sheet and no further adjustments to their valuation are made. Some of our warrants were determined to be ineligible for equity classification because of provisions that may result in an adjustment to their exercise price. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as assets or liabilities are recorded on our consolidated balance sheet at their fair value on the date of issuance and are revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. We estimate the fair value of these assets/liabilities using option pricing models that are based on the individual characteristics of the warrants or instruments on the valuation date, as well as assumptions for expected volatility, expected life and risk-free interest rate. Changes in the assumptions used could have a material impact on the resulting fair value. The primary input affecting the value of our derivatives liabilities is the Company s stock price. For example, at September 30, 2012, a 50% change in the value of the Company s stock price would affect the value of the derivative liability by approximately $0.3 million to $0.4 million, depending on other inputs.

Reverse Stock Split

As of November 17, 2011, the Company effected a 1 for 10 reverse stock split (the reverse stock split). As a result of the reverse stock split, each ten shares of the Company s Common Stock issued and outstanding immediately prior to the reverse split was combined into one share of Common Stock. Also, as a result of the Reverse Stock Split, the per share exercise price of, and the number of shares of Common Stock underlying outstanding Company stock options, warrants, Series A Preferred and any Common Stock based equity grants outstanding immediately prior to the reverse stock split was proportionally adjusted, based on the one-for-ten split ratio, in accordance with the terms of such options, warrants or other Common Stock based equity grants as the case may be. No fractional shares of Common Stock were issued in connection with the reverse stock split. Stockholders instead received cash payment in lieu of any fractional shares. Unless otherwise noted, all share and per share amounts in these have been retrospectively adjusted to reflect the reverse stock split.

Full Year Review

On October 21, 2011, the Company acquired Roche Madison, Inc. and other intangible assets from Roche. The acquisition included a laboratory research facility in Madison, Wisconsin comprising over 24,000 square feet. Roche Madison Inc. employed 41 employees at the time of the acquisition. Due to the significant new costs associated with the facility, its people and research programs, salary costs, general and administrative costs, and research and development costs increased significantly relative to prior periods. Going forward, we expect this increased cost structure to continue as research and development efforts are accelerated.

On April 11, 2012, the Company acquired Alvos Therapeutics, Inc., a targeted therapeutics company. Prior to the acquisition, Alvos licensed a large platform proprietary human-derived Homing Peptides and the method for their discovery from MD Anderson Cancer Center. The company hired one employee as a result of the acquisition, and the operations of Alvos are being integrated into our research facility in Madison, Wisconsin.

Results of Operations

The Company had a net loss of $22.1 million for the year ended September 30, 2012, compared to a net loss of $3.5 million for the year ended September 30, 2011, an increase of $18.6 million.

The change in the net loss was the result of a number of factors. During the year ended September 30, 2011, the Company recognized income from discontinued operations of $5.4 million related to the gain on disposal of Unidym, which was not repeated in the current period. In fiscal 2012, the Company recorded an impairment charges and recorded as reserve against a receivable from its unconsolidated affiliates, in the amount of $4.1 million. In fiscal 2012, the company recorded a loss on disposal of equipment of $1.1 million, related to non-strategic equipment obtained in conjunction with the acquisition of Roche Madison, and subsequently sold. These losses were partially offset by a gain recorded on the acquisition of Roche Madison of $1.6 million. All of these items are non-operating, one-time occurrences. However, research and development costs increased significantly in the current fiscal year due to the acquisition of Roche Madison, its facility costs, personnel costs, and program costs. Details of the results of operations are presented below.

Revenues

The Company generated revenue of $147,000 during the year ended September 30, 2012, due to license agreements obtained in conjunction with the acquisition of Roche Madison, as compared to revenue of $296,000 during the year ended September 30, 2011. The revenue in 2011 was primarily related to a qualifying therapeutic discovery grant received by Calando.

Operating Expenses

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. For purposes of comparison, the amounts for the years ended September 30, 2012 and 2011 are shown in the table below.

Salary & Wage Expenses Fiscal 2012 compared to Fiscal 2011

The Company employs management, administrative, and scientific and technical staff at its corporate offices and its research facility. Salaries and wages expense consists of salary and related benefits. Salary and benefits include two major categories: general and administrative compensation expense, and research and development compensation expense, based on the primary activities of each employee. The following table provides detail of salary and related benefits expenses for the years ended September 30, 2012 and 2011.

(in thousands)

	Twelve months Ended September 30, 2012	% of Expense Category	Twelve months Ended September 30, 2011	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
G&A compensation-related	$ 3,107	48%	$ 1,144	81%	$ 1,963	172%
R&D compensation-related	3,308	52%	264	19%	3,044	1153%
Total	$ 6,415	100%	$ 1,408	100%	$ 5,007	356%

During the year ended September 30, 2012, G&A compensation expense increased $1,963,000. During the fiscal year, upon the acquisition of Roche Madison, the Company expanded its senior management team. Its G&A headcount also increased due to several Madison employees classified as G&A. During the year ended September 30, 2012, R&D compensation expense increased $3,044,000. This increase was due to employees hired upon the acquisition of Roche Madison.

General & Administrative Expenses Fiscal 2012 compared to Fiscal 2011

The following table provides details of our general and administrative expenses for the fiscal years 2012 and 2011.

(in thousands)

	Twelve months Ended September 30, 2012	% of Expense Category	Twelve months Ended September 30, 2011	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Professional/outside services	$ 1,800	28%	$ 2,383	63%	$ (583)	-24%
Patent expense	1,024	16%	604	16%	420	70%

Facilities and related	120	2%	168	4%	(48)	-29%
Travel	369	6%	201	5%	168	84%
Business insurance	202	3%	194	5%	8	4%
Communication and Technology	196	3%	96	3%	100	104%
Office expenses	91	1%	54	1%	37	69%
Other	2,637	41%	95	3%	2,542	NM
Total	$ 6,439	100%	$ 3,795	100%	$ 2,644	70%

Professional/outside services include legal, accounting and other outside services retained by Arrowhead and its subsidiaries. All periods include normally occurring legal and accounting expenses related to SEC compliance and other corporate matters. Professional/outside services expense was $1,800,000 during the year ended September 30, 2012, compared to $2,383,000 in the comparable prior period. In the prior period, the Company recorded expenses of $663,000 related to stock issued for financing commitments in association with the September 2011 financing in conjunction with the acquisition of Roche Madison, Inc.

Patent expense was $1,024,000 during the year ended September 30, 2012, compared to $604,000 in the comparable prior period. During the year ended September 30, 2012, approximately half of the patent expense was related to fees paid to patent counsel for the maintenance of newly acquired intellectual property in conjunction with the acquisition of Roche Madison. The balance of patent expense primarily relates to Calando s intellectual property portfolio, and to a lesser extent the intellectual property acquired in conjunction with the Alvos acquisition and the Ablaris patent portfolio. The Company expects to continue to invest in patent protection as the Company extends and maintains protection for its current portfolios and files new patent applications as its product applications are improved.

Facilities and related expense was $120,000 during the year ended September 30, 2012, compared to $168,000 in the comparable prior period. Facilities and related expense within general and administrative expenses primarily relate to rental costs associated with the Company s headquarters in Pasadena, California. Facilities expense decreased due to reduction in the company s rental expense because its lease for its corporate headquarters expired. During most of fiscal 2012, the Company occupied smaller and less expensive office space. In August 2012, the Company moved into a new facility. Its rental costs in fiscal 2013 are expected to increase relative to the temporary space occupied in 2012.

Travel expense was $369,000 during the year ended September 30, 2012, compared to $201,000 in the comparable prior period. Travel expense increased due to travel associated with the acquisition of Roche Madison Inc., as well as additional travel costs related to Madison-based employees. During fiscal 2012, the Company hired a Chief Operating Officer and a Chief Business Officer, whose job functions require travel. Also, travel costs are expected to increase in the future due to increased travel between the Madison and Pasadena locations. Travel expense includes costs related to travel by Company personnel for operational business meetings at other company locations, business initiatives and collaborations throughout the world with other companies, marketing, investor relations, fund raising and public relations purposes. Travel expenses can fluctuate from quarter to quarter and from year to year depending on current projects and activities.

Business insurance expense was $202,000 during the year ended September 30, 2012, compared to $194,000 in the comparable prior period. The company experienced favorable rate decreases in its Directors and Officers insurance coverage, which was offset by additional insurance costs associated with Madison.

Communication and technology expense was $196,000 during the year ended September 30, 2012, compared to $96,000 in the comparable prior period. The increase was related to software maintenance costs at Madison, primarily desk top software and license renewal fees on software related to the operation of laboratory equipment.

Office expenses are administrative costs to facilitate the operations of the Company s office facilities in Pasadena and Madison, and include office supplies, copier/printing costs, postage/delivery, professional dues/memberships, books/subscriptions, staff amenities, and professional training. Office expenses were $91,000 during the year ended September 30, 2012, compared to $54,000 in the comparable prior period. The increase in office expenses was related to costs incurred at its newly acquired Madison facility.

Other expense was $2.6 million during the year ended September 30, 2012 compared to $95,000 in the comparable prior period. During the year ended September 30, 2012, the Company recorded reserves against receivable from its unconsolidated affiliates, Nanotope and Leonardo in the amount of $2.5 million.

Research and Development Expenses Fiscal 2012 compared to Fiscal 2011

R&D expenses are related to the Company s on-going research and development efforts, primarily related to its laboratory research facility in Madison, Wisconsin, and also include outsourced R&D services. The following table provides detail of research and development expense for the years ended September 30, 2012 and 2011.

(in thousands)

	Twelve months Ended September 30, 2012	% of Expense Category	Twelve months Ended September 30, 2011	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Outside labs & contract services	$ 1,096	20%	$ 605	19%	$ 491	81%
In vivo studies	302	6%	29	1%	273	941%
Drug Manufacturing	1,256	23%	68	2%	1,188	1747%
Consulting	655	12%	440	13%	215	49%
License, royalty & milestones	274	5%	2,045	63%	(1,771)	-87%
Laboratory supplies & services	793	15%	2	0%	791	NM
Facilities and related	787	15%	8	0%	779	NM
Sponsored research	185	3%	75	2%	110	147%
Other research expenses	43	1%	6	0%	37	617%
Total	$ 5,391	100%	$ 3,278	100%	$ 2,113	64%

Outside lab and services expense was $1,096,000 during the year ended September 30, 2012, compared to $605,000 in the comparable prior period. The increase is due to outside services contracted to complement the research performed at our Madison facility, which was acquired in October 2012, and not part of the prior period expenses.

In vivo studies expense was $302,000 during the year ended September 30, 2012, compared to 29,000 in the comparable prior period. The current period expense relates to preclinical animal studies at our Madison research facility, and we expect this increased level of expense for such studies to continue at an elevated level as the company accelerates its product development efforts. The prior period expense related to certain limited outsourced in vivo studies related to Calando.

Drug manufacturing expense was $1,256,000 during the year ended September 30, 2012, compared to $68,000 in the comparable prior period. Approximately half of the drug manufacturing expense related to raw materials, specifically, polymer components for RONDEL. Prior year costs for this program were $68,000. The other half of the drug manufacturing costs relate to our manufacturing campaign related to the Company s Hepatitis B Virus (HBV) program, which began in the fourth quarter of fiscal 2012, for use in upcoming GLP toxicity studies planned in the first half of fiscal 2013. The Company is utilizing outside manufacturers to produce these components; these costs will continue until the manufacturing campaign is completed in 2013.

Consulting expense was $655,000 during the year ended September 30, 2012, compared to $440,000 in the comparable prior period. The increase in consulting expense was primarily related to fees paid to our consultants monitoring our clinical trial at Calando, as well as clinical consulting costs for a planned clinical trial in HBV, as well as higher costs associated with the scientific advisory board at Ablaris.

License, royalty & milestone expense was $274,000 during the year ended September 30, 2012, compared to $2,045,000 in the comparable prior period. The licensing fees, royalty and milestones expenses during the prior year reflect a one-time to $2 million in licensing fees paid to University of Texas M.D. Anderson Cancer Center for the anti-obesity compound licensed by Ablaris. The current year expense also relates to Ablaris and was payable to the University of Texas M.D. Anderson Cancer Center related to a milestone achieved by dosing its first patient in an obesity/prostate cancer clinical trial.

Stock-based compensation expense

Stock-based compensation expense, a noncash expense, was $1,241,000 during the year ended September 30, 2012, compared to $1,376,000 during the comparable prior period. Stock-based compensation expense is based upon the valuation of stock options granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company s stock price on the date of the grant, as well as other assumptions. Based on the completion of vesting of a number of stock options during the second half of fiscal 2011, compensation expense related to those awards ended. This was mostly offset by additional options granted to new and existing employees in fiscal 2012.

Depreciation and amortization expense

Depreciation and amortization expense, a noncash expense, was $1,749,000 during the year ended September 30, 2012, compared to $268,000 during the comparable prior period. The majority of depreciation and amortization expense relates to depreciation on lab equipment obtained as part of the acquisition of Roche Madison. In addition, the Company records depreciation on leasehold improvements at its Madison research

facility. The Madison facility was acquired in October 2011; therefore, there was no related depreciation in the prior year. Finally, certain patents acquired previously have been capitalized and amortized over the remaining useful lives of the respective patents.

Other Income / Expense

Other income / expense changed from income of $1,045,000 in fiscal 2011 to other expense of $1,021,000 in fiscal 2012. During fiscal 2012, the Company recorded several nonrecurring items: Impairment of its investment in its unconsolidated affiliate, Nanotope of $1.4 million, a loss on the disposal of fixed assets of $1.1 million, and a gain recorded upon the acquisition of Roche Madison of $1.6 million, and an impairment of its investment in Leonardo of $0.2 million. Other component of other income/expense was the change in value of derivatives, which was $387,000 in fiscal 2012, compared to $1.1 million in fiscal 2011.

Liquidity and Cash Resources

As a development stage company, Arrowhead has historically financed its operations through the sale of securities of Arrowhead and its Subsidiaries. Research and development activities have required significant capital investment since the Company s inception, and are expected to continue to require significant cash investment in fiscal 2012.

At September 30, 2012, the Company had cash on hand of approximately $3.4 million. In addition, the Company had subscriptions receivable from previous financings of $1.0 million, and a short term note receivable of approximately $2.4 million. Cash and cash equivalents decreased $4.1 million during fiscal 2012 from $7.5 million at September 30, 2011 to $3.4 million at September 30, 2012.

Cash used in operating activities was $16.0 million, which represents the on-going expenses of its research and development programs, and corporate overhead. Cash outlays were primarily composed of the following: salary and payroll-related costs was $6.5 million, general and administrative costs were $4.0 million, research and development costs were $4.8 million. $0.9 million was used to fund operating expenses at Arrowhead s two minority interest companies, Nanotope and Leonardo. Cash expenses were somewhat offset by cash received from revenues of $0.2 million.

Cash provided by investing activities was $0.4 million, primarily related to cash received from the sale of investments of $0.5 million, proceeds from the disposal of fixed assets of $0.3 million, offset by capital expenditures of $0.5 million.

Cash provided by financing activities of $10.8 million includes $11.0 million received related to cash received from the sale of Common Stock, offset by principal payments on capital leases of $0.2 million.

These matters raise substantial doubt about the Company s ability to continue as a going concern. These financial statements were prepared under the assumption that the Company will continue as a going concern and do not include any adjustments that might result from the outcome of that uncertainty.

Recent Financing Activity / Sources of Capital:

In December 2012, the Company sold 1.9 million units at a price of $2.26 per unit in a public offering. Each unit consisted of one share of Common Stock and a warrant to purchase 0.5 share of Common Stock, exercisable at $2.20. Gross proceeds from the offering were $4.3 million, which included a $500,000 promissory note due February 1, 2013. Commissions and other offering expenses are expected to be approximately $300,000.

On August 10, 2012, the Company sold 2.3 million units at a price of $2.76 per unit in a registered offering to institutional and individual investors. Each unit consisted of one share of Common Stock and a warrant to purchase 0.75 share of Common Stock exercisable at $3.25 per share. Gross proceeds from the offering were approximately $6.2 million, with net proceeds of approximately $5.8 million after deducting commissions and other offering expenses.

On September 30, 2011, the Company sold 1,458,917 shares of Common Stock at a price of $3.80 per share. Cash proceeds received in fiscal 2011 were $4.6 million, cash proceeds in the first six months of fiscal 2012 were $0.4 million, and the balance is expected to be received in 2012. On October 4, 2011, the Company completed a second closing to the offering in which the Company sold 138,158 shares of Common Stock at a price of $3.80 per share. Cash proceeds were $525,000.

On October 20, 2011, the Company and Lincoln Park Capital Fund, LLC, an Illinois limited liability company (LPC) entered into a $15 million purchase agreement, together with a registration rights agreement, whereby LPC agreed to purchase up to $15 million of Common Stock, subject to certain limitations, from time to time during the three-year term of the agreement. Additionally, the Company filed a registration statement with the U.S. Securities & Exchange Commission covering the resale of the shares that may be issued to LPC under the agreement. On January 30, 2012, the SEC declared the registration statement effective for the resale of such shares. The Company has the right, in its sole discretion, over a 36-month period to sell up to $15 million of Common Stock (subject to certain limitations) to LPC, depending on certain conditions as set forth in the agreement. As of September 30, 2012, the Company had drawn $1 million from the facility.

Although the Company has sources of liquidity, as described above, the Company anticipates that further equity financings, and/or asset sales and license agreements will be necessary to continue to fund operations in the future.

Off-Balance Sheet Arrangements

As of September 30, 2012, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of SEC Regulation S-K.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a Smaller Reporting Company, we are not required to provide this information.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this item is included in Item 15 of this Annual Report Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Our Chief Executive Officer and our Chief Financial Officer, after evaluating our disclosure controls and procedures (as defined in Securities Exchange Act of 1934 (the Exchange Act) Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Annual Report on Form 10-K (the Evaluation Date) have concluded that as of the Evaluation Date, our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms, and to ensure that information required to be disclosed by us in such reports is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer where appropriate, to allow timely decisions regarding required disclosure.

Management s Annual Report on Internal Control over Financial Reporting

Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States. This process includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the internal control over financial reporting to future periods are subject to risk that the internal control may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Management s Assessment of the Effectiveness of our Internal Control over Financial Reporting

Management has evaluated the effectiveness of our internal control over financial reporting as of September 30, 2012. In conducting its evaluation, management used the framework set forth in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on our evaluation under such framework, management has concluded that our internal control over financial reporting was effective as of September 30, 2012.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the fourth quarter of the year ended September 30, 2012, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.
Board of Directors:

The names and ages of our directors serving as of December 14, 2012 are provided below. Directors are elected annually for a one year term. Biographical information regarding these officers is set forth under the following table.

Name	Age	Position with Arrowhead
Christopher Anzalone	43	Chief Executive Officer & President and Director
Douglass Given	60	Chairman of the Board
Mauro Ferrari	53	Director
Edward W. Frykman	76	Director
Charles P. McKenney	74	Director