

ARROWHEAD RESEARCH CORP

Form 10-K

December 15, 2008

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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

**FORM 10-K**

(Mark One)

**ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended September 30, 2008.

**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)

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**Delaware**  
(State of incorporation)

**46-0408024**  
(I.R.S. Employer Identification No.)

**201 S. Lake Avenue, Suite 703**

**Pasadena, California 91101**

**(626) 304-3400**

(Address and telephone number of principal executive offices)

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

<b>Title of each class</b>	<b>Name of each exchange on which registered</b>
<b>Common Stock, \$0.001 par value</b>	<b>The NASDAQ Global Market</b>

**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

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

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  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.

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

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

Issuer's revenue for its most recent fiscal year: \$1,303,201.

The aggregate market value of issuer's outstanding Common Stock held by non-affiliates was approximately \$107.5 million based upon the bid price of issuer's Common Stock on March 31, 2008.

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As of December 11, 2008, 42,934,517 shares of the issuer's Common Stock were outstanding.

### **DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement for fiscal year ended September 30, 2008, expected to be filed with the Commission no later than January 28, 2009, for the registrant's 2008 Annual Meeting of Stockholders to be held March 12, 2009, are incorporated by reference into Part III of this report.

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**SPECIAL NOTE REGARDING 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 undertake no obligation 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.*

**WHERE YOU CAN FIND MORE INFORMATION**

As a public company, we are required to file annual, quarterly, and current reports, proxy statements and other information with the SEC. You may read and copy any of our materials on file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, DC 20549, as well as at the SEC's regional office at 5757 Wilshire Boulevard, Suite 500, Los Angeles, California 90036. Our filings are available to the public at the SEC's website at [www.sec.gov](http://www.sec.gov). Please call the SEC at 1-800-732-0330 for further information on the Public Reference Room. We also provide copies of our Forms 8-K, 10-K, 10-Q, Proxy Statements and Annual Reports at no charge to investors upon request and make electronic copies of our most recently filed reports available through our website at [www.arrowheadresearch.com](http://www.arrowheadresearch.com) as soon as reasonably practicable after filing such material with the SEC.

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**PART I**

**ITEM 1. BUSINESS**

***Description of Business***

*Unless otherwise noted, (1) the term Arrowhead refers to Arrowhead Research Corporation, a Delaware corporation formerly known as InterActive Group, Inc., (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 the company Arrowhead, (3) the term ARC refers to Arrowhead Research Corporation, a privately-held California corporation with which Arrowhead consummated a stock exchange transaction in January 2004, (4) the term Subsidiaries refers collectively to Calando Pharmaceuticals, Inc., Unidym, Inc., Agonn Systems, Inc. and Tego Biosciences Corporation and (5) the term Common Stock refers to Arrowhead's Common Stock and the term stockholder(s) refers to the holders of Common Stock or securities exercisable for Common Stock.*

***Overview***

Arrowhead is a nanotechnology holding company striving to bring new products to market via its subsidiaries and investments in the healthcare, electronics, and clean energy industries. Our mission is to create shareholder value by building Subsidiaries that may be monetized in three primary ways: (1) Subsidiaries may be sold to other companies with proceeds flowing back to Arrowhead; (2) Subsidiaries may execute an IPO, with proceeds flowing back to Arrowhead and/or providing Arrowhead with tradable stock; and (3) Subsidiaries may become mature operating units with earnings consolidated with Arrowhead. In the near-term, we are focused on maximizing the value of our most mature Subsidiaries, Calando Pharmaceuticals, Inc. and Unidym, Inc., through internal development, partnership and license arrangements, as well as pursuing new sources of cash investments. Our longer-term strategy for development and investment in existing Subsidiaries and minority investments will be determined by cash availability and the strength of technology and market opportunity. Arrowhead is continually identifying and developing business opportunities for new areas of investment which may be engaged as capital resources allow.

Arrowhead has created a scalable platform on which to build highly specialized subsidiaries with an eye to maximizing capital efficiency and accelerating the rate of product development. Our subsidiaries are built around university-derived technologies and by acquisition of existing companies. Arrowhead is highly active in the operation of its subsidiaries, providing initial management, operational support, business development and financing. We believe the combination of these strategies is advantageous and unique for a single institution and that it provides unique advantages to Arrowhead's stockholders. Arrowhead's approach is designed to give its Subsidiaries and investments an edge in commercializing nanotechnologies by allowing Subsidiary management both guidance and the freedom to focus on the development and marketing of their technologies by providing key services to its Subsidiaries.

Arrowhead currently operates two majority-owned Subsidiaries, two wholly owned Subsidiaries and has minority investments in two early stage nanotechnology companies focused on developing and commercializing nanotech products and applications, including anti-cancer drugs, RNAi therapeutics, regenerative therapeutics, advanced drug delivery technology, energy storage technology, and carbon-based electronics.

The Company was originally incorporated in South Dakota in 1989, and was reincorporated in Delaware in 2000 under the name InterActive, Inc. ( InterActive ). On January 12, 2004, InterActive consummated a stock exchange transaction with the owners of ARC, a privately-held California corporation. This transaction is referred to as the Share Exchange. Upon consummation of the Share Exchange, the owners of ARC acquired approximately 89% of the Common Stock of the Company. InterActive changed its name to Arrowhead Research Corporation and ARC was subsequently dissolved. The Company's principal executive offices are located at 201 South Lake Avenue, Suite 703, Pasadena, California 91101, and its telephone number is (626) 304-3400. As of September 30, 2008, Arrowhead Research Corporation had 15 full-time employees at the corporate office and 53 full-time employees at its Subsidiary companies.

**Table of Contents*****Subsidiaries and Investments***

The Company's two majority-owned Subsidiaries, two wholly owned Subsidiaries and two minority investments are focused on developing and commercializing a variety of nanotechnology products and applications, including anti-cancer drugs, RNAi therapeutics, regenerative therapeutics, advanced drug delivery technology, energy storage technology, carbon-based electronics, and fullerene anti-oxidants. Arrowhead anticipates expanding its portfolio through selective acquisition and the formation of new companies, as capital resources allow.

As of September 30, 2008, Arrowhead held a majority of the outstanding voting stock of the following four Subsidiaries and minority interests in two additional companies.

<b>Subsidiary</b>	<b>% Ownership</b>	<b>Technology/Product Focus</b>
Calando Pharmaceuticals, Inc. <i>acquired June 4, 2004</i>	67.8%	Clinical stage nano-engineered delivery of RNAi therapeutics and small molecule drugs for the treatment of cancer with first anti-cancer compound
Unidym, Inc. (formerly NanoPolaris) <i>founded April 4, 2005</i>	53.8%	Commercialization of carbon nanotube products for the electronics industry
Tego Biosciences Corporation <i>acquired April 20, 2007</i>	100.0%	License and partnership of technology related to modification of fullerenes for therapeutic and diagnostic applications
Agonn Systems, Inc. <i>founded May 1, 2008</i>	100.0%	Developing nanotechnology based energy storage devices for hybrid electric vehicles and other large format applications

\* Each of Calando, Unidym and Tego has an option plan to help motivate and retain employees. Calando has 4,335,473 outstanding warrants, primarily issued in connection with a financing event that closed in October 2006. As of September 30, 2008, assuming all options in each of Calando, Unidym and Tego were awarded and exercised and all warrants were exercised, the Company would own approximately 63.6% of Calando, 37.8% of Unidym, 80% and Tego. Agonn has not yet adopted an option plan and does not have any outstanding warrants.

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<b>Minority Investment</b>	<b>% Ownership<sup>1</sup></b>	<b>Technology/Product Focus</b>
Nanotope, Inc	22%	Developing nano-engineered, self-assembling, bioactive scaffolding for the treatment of spinal cord injury and peripheral artery disease
Leonardo Biosystems, Inc.	6%	Developing an advanced set of nanotechnology tools to deliver anti-cancer therapeutics

\* In April 2008, Arrowhead acquired Masa Energy LLC, a limited liability company whose sole assets were an approximately 6% ownership position in each Nanotope, Inc. and Leonardo Biosystems, Inc. Arrowhead invested \$2 million in Nanotope in two tranches of \$1 million in July 2008 and \$1 million in September 2008 which brought Arrowhead's ownership in Nanotope to 22%.

**Cash Resources**

As a development stage company, Arrowhead has historically financed its operations through the sale of securities of Arrowhead and its Subsidiaries. Development of products at our Subsidiaries, in particular Calando and Unidym, has required significant capital investment since the Company's inception in 2003 and will continue to require significant cash investment in fiscal 2009 for the Company to fund operations at historical levels. At September 30, 2008, Arrowhead had cash on hand of approximately \$10 million on a consolidated basis. The Company recognizes that if no additional cash resources are obtained, the Company must scale back its cash consumption to remain a going concern.

The Board has approved a strategy for the Company to conserve cash and seek sources of new capital. To execute this strategy, the Board will seek to accomplish one or more of the following on favorable terms:

out-license of technology;

sale of a subsidiary;

sale of non-core assets;

funded joint development or partnership arrangements; and

sale of securities.

The Company is actively involved in discussions with third parties regarding many of these alternatives. Until such time as one or more of these goals is accomplished, the Company will continue to implement streamlining and cash conservation measures begun in fiscal 2008 and defer major investment in new initiatives. If no additional cash is obtained by mid second quarter 2009, the Company has a plan to make even deeper cuts in its development efforts at Calando and Unidym and reduce expenses at Arrowhead so that the Company has cash to fund operations in a limited manner through fiscal 2009 and into fiscal 2010. See Risk Factors beginning on page 15.

**Subsidiaries**

*Calando Pharmaceuticals, Inc.*

**Liquidity**

In the second quarter of fiscal 2008, the Company merged two majority owned Subsidiaries, Insert Therapeutics, Inc. and Calando to bring both drug delivery platforms into the same company. The merged company is operating under the name Calando Pharmaceuticals, Inc. At the same time, Calando shifted focus from preclinical and pipeline development to emphasize its clinical program. Consequently, Calando's operations were streamlined by reductions in executive and technical staff and the facilities for the two companies were consolidated. In connection with



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the reduction in Calando's executive management, Arrowhead took over the management of Calando. These actions reduced the consumption of cash for salaries and facilities. However, significant cash was consumed in fiscal 2008 in preparation of an IT-101 Phase II clinical trial, the CALAA-01 Phase I clinical trial, and the development of a second RNAi therapeutic. Since the merger in April 2008, Arrowhead has made a series of cash advances totaling approximately \$5 million to fund Calando's operations. Subsequent to September 30, 2008, Calando has signed agreements to issue \$2.7 million in senior unsecured convertible promissory notes with a two-year maturity of which \$1.1 million has been received, and is seeking to raise an additional \$2.3 million under the same terms. Calando's cash consumption fluctuates from quarter to quarter depending on the progress of its projects, but in fiscal 2008, it has ranged between \$2.2 million and \$2.6 million per quarter. If Calando is unsuccessful in attracting additional capital and Arrowhead does not have sufficient cash resources to support Calando's operations, some or all of Calando's development projects would have to be scaled back, interrupted, or abandoned in order to manage cash that Calando can operate in a limited manner through fiscal 2009 and into fiscal 2010.

### General

The Company believes that Calando is an attractive near term partnership candidate or acquisition target for several pharmaceutical and biotech companies that are active in the development of RNAi therapeutics. Systemic delivery has posed a major hurdle to the clinical development of siRNA therapeutics. Calando is in ongoing discussions with multiple potential partners and acquirers.

Calando is Arrowhead's most mature biopharmaceutical Subsidiary. Calando's technology and products are based on technology developed at the California Institute of Technology. Calando utilizes modified cyclodextrin molecules as building blocks to create an entirely new class of drug delivery materials: linear cyclodextrin-containing polymeric nanoparticles ( **LCDPs** ). Calando's proprietary linear cyclodextrin nanoparticle technology is designed to deliver small molecule drugs using Calando's Cyclosert™ system and RNAi therapeutics using the RONDEL™ system. Using these platform systems, Calando has developed two anti-cancer drug candidates that are currently undergoing human clinical trials.

By combining small molecule drugs, nucleic acids (i.e., microRNA or siRNA) or peptides with our Cyclosert polymers, Calando believes it can significantly improve the targeting, solubility, stability, toxicity, efficacy and pharmacokinetic profile of therapeutic compounds. Calando's LCDP nanoparticle platform technologies ( **Cyclosert™ and RONDEL™** ) actively facilitate the directed transport, efficient uptake and controlled release of therapeutic payloads. Additionally, cell surface receptor ligands can also be attached to our delivery system to provide for targeted delivery of therapeutic agents directly to tumor cells or to other selected tissues. Studies done by Calando and others have demonstrated the importance of therapeutic targeting in eliciting a desired therapeutic effect.

Calando's first small molecule/nanoparticle conjugate drug candidate, IT-101, began clinical trials in July 2006. IT-101 is a conjugate of Cyclosert and the anti-cancer agent, Camptothecin ( **CPT** ). Camptothecin is a potent anti-cancer agent that was never commercialized mainly due to its devastating side effects, instability in the bloodstream and insolubility. By combining Camptothecin with Cyclosert, the solubility, stability, toxicity profile, biodistribution and pharmacokinetics of Camptothecin have been significantly improved as shown in Calando's phase I clinical trial. Results of in vivo studies in tumor-bearing mice demonstrate that Calando's Cyclosert enhanced Camptothecin conjugate ( **IT-101** ) has significantly greater anti-tumor activity than its analog anticancer agent, irinotecan, marketed by Pfizer as Camptosar®. In Phase I clinical studies, IT-101 demonstrated safety and multiple patients with extended progression free survival, and was not associated with the severe hematological and gastrointestinal toxicities associated with Camptosar.

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CALAA-01 is Calando's first nanoparticle drug candidate delivering siRNA. CALAA-01 is a targeted nanoparticle, comprised of a proprietary, non-chemically-modified siRNA against the M2 subunit of ribonucleotide reductase—a clinically-validated cancer target—formulated with our proprietary RONDEL (RNAi/Oligonucleotide Nanoparticle Delivery) polymer delivery system. CALAA-01 is the first drug delivery system enabled siRNA therapeutic to enter clinical trials. The drug is currently in a dose escalation phase I clinical trial at UCLA and the START Clinic in San Antonio.

### **The Drug Delivery and Oncology Markets**

Despite advances in drug discovery, pharmaceutical firms remain challenged by getting the right compound to the right place in the human body, where it can maximize effect. Additionally, over the next decade, multiple "blockbuster" pharmaceuticals will go off patent, resulting in a significant loss to the pharmaceutical industry as generics enter the market. Patent expiration coupled with a challenging drug discovery environment, and continued problems with late stage trial failures has left pharmaceutical pipelines thin. In response, the industry has pursued reformulation of existing or previously failed compounds using new drug delivery technology to expand pipelines and prolong patent life. The global drug delivery market for all delivery technologies is expected to exceed \$67B by 2009.<sup>1</sup> The market for targeted delivery of small molecule pharmaceuticals using particulate/liposomal delivery systems is estimated to grow to \$4.8B in 2012.<sup>2</sup> According to the American Cancer Society, cancer is the second leading cause of death in the United States and accounts for approximately one in every four deaths. The National Institutes of Health has estimated the direct medical cost of cancer to be in excess of \$74 billion per year. Dose limiting toxicity, poor tissue specificity, and large effective distribution are major restrictive factors in effective cancer chemotherapy. Consequently, complete tumor response is not often achieved in patients receiving chemotherapy alone. This offers a potential for significant opportunity for firms developing technologies to more effectively deliver anti-cancer agents to malignant cells.

### **Calando Pharmaceuticals Platform Technologies**

#### ***Cycloset Nanoparticles***

Cycloset links potent therapeutics to linear, cyclodextrin-based polymers to generate macromolecular prodrugs. Cyclodextrins are cyclical sugars that are highly water soluble but contain a hydrophobic cavity enabling the formation of complexes with insoluble molecules. Functionalized cyclodextrins are biocompatible and non-immunogenic, resist degradation by human enzymes and are non-toxic, resulting in their use in many pharmaceutical formulations. Preclinical and clinical studies show that Cycloset retains all of these characteristics of cyclodextrin while providing unprecedented additional functionality. The components of Cycloset undergo a highly reproducible, proprietary self-assembly process resulting in nanoparticles with close to neutral surface charge. This assembly is mediated by the presence of the drug on the polymer.

Data from our preclinical as well as clinical research indicate that Cycloset have been observed to have the following advantages over traditional chemotherapeutics:

*High solubility without the need for additional solubilizing agents*

*Increased circulation half-life*

*Tumor accumulation*

*Protection of drugs from enzymatic degradation*

*Stealthy to the immune system*

*Non-toxic polymer carrier*

- <sup>1</sup> [www.nanomarkets.net](http://www.nanomarkets.net)
- <sup>2</sup> SkyePharma 10Q, [www.skyepharma.com](http://www.skyepharma.com)

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*Stable under physiological conditions*

*Significant improvement in therapeutic index compared to the active molecule alone. This may result in improved quality of life and better efficacy due to on-time administration with fewer dose reductions or limitations on the optimal number of therapy cycles.*

### **RONDEL Nanoparticles:**

RNA interference, or RNAi, is a naturally occurring mechanism within cells that selectively silences and regulates specific genes. Since many diseases are caused by the inappropriate activity of specific genes, the ability to silence genes selectively through RNAi could provide a new way to treat a wide range of human diseases. RNAi is induced by small, double-stranded RNA molecules. One method to activate RNAi is with chemically synthesized small interfering RNAs, or siRNAs, which are double-stranded RNAs that are targeted to a specific disease-associated gene. The siRNA molecules are used by the natural RNAi machinery in cells to cause highly targeted gene silencing. A key roadblock to the therapeutic use of RNAi is the lack of an effective delivery mechanism. siRNA is degraded and destroyed in the bloodstream if unprotected and naked siRNA is not taken up by cells.

Calando addresses the RNAi delivery issue with its targeted, cyclodextrin-containing polymers that form the foundation for the RONDEL delivery technology. The first component is a cyclodextrin-containing polycation that, when mixed with siRNA, binds to the anionic backbone of the siRNA. The polymer and siRNA self-assemble into nanoparticles of approximately 50-70 nm diameter that fully 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 through proprietary linkages.

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. Ligands to cell surface receptors can be covalently attached to the adamantane-PEG modifier, enabling the siRNA-containing particles to be targeted to tissues of interest. Numerous ligand types (e.g., small molecules, peptides, proteins) can be used.

The RONDEL system has been designed for use as part of a two-vial system: one vial contains the foregoing delivery components, and the second vial containing the therapeutic siRNA payload. When mixed pursuant to a simple protocol, the particles self-assemble into the nanoparticles as described above. The RONDEL delivery system has been designed for intravenous injection. Upon delivery to the target cell, the targeting ligand binds to membrane receptors on the cell surface and the RNA-containing nanoparticle is taken into the cell by endocytosis. There, the polymer functions to unpackage the siRNA from the delivery vehicle.

### **Clinical Development Programs**

#### **IT-101: Cycloset-enhanced Camptothecin**

Calando's lead small molecule drug candidate is IT-101. IT-101 is comprised of Cycloset conjugated with the anticancer compound CPT for systemic treatment of both primary and metastatic solid tumors. The primary target of IT-101 is topoisomerase I (Topo I), an enzyme essential to mammalian DNA replication. CPT and its derivatives, such as topotecan and irinotecan, face a number of pharmacologic challenges that IT-101 was designed to address: (i) it provides high intratumoral drug concentrations for extended periods of time, keeping the reversible cleavage complex between Topo I and CPT from dissociating, (ii) it minimizes plasma free CPT concentrations thereby reducing the severity of side effects such as diarrhea and severe neutropenia observed with other CPT analogs, and (iii) it prevents the degradation of CPT to its inactive, open-ring (carboxylate) form.

Additionally, recent studies illustrate that low-dose and increased frequency of CPT administration results in a down-regulation of hypoxia-inducible factor 1 (HIF-1) with a sustained inhibition of tumor growth independent of DNA breaks. The IT-101 development program is specifically designed to take full advantage of these mechanisms of action by providing linear delivery of CPT for prolonged periods with a low plasma free-CPT concentration; thus avoiding the toxicity observed with traditional non-polymerized topoisomerase inhibitors.

Calando completed clinical trials with IT-101 at the City of Hope Cancer Center (COH) in Duarte, California in October 2008. The trial was an open-label, dose-escalation Phase I study in patients with unresectable or metastatic solid tumors refractory to other therapies. Initially, the trial utilized a weekly dosing schedule. A subsequent Phase Ib

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study was conducted utilizing a twice monthly dosing schedule. All trial endpoints have been successfully achieved. The drug was found to be well tolerated in both the Phase Ia and Ib studies of the trial. A high proportion of patients displayed stable disease following treatment thereby showing evidence of IT-101's cytostatic activity. This activity is consistent with several published clinical studies reporting improved outcomes when lower doses of topotecan were administered on a continuous regimen compared to traditional intermittent schedules. Topotecan is an FDA-approved cytotoxic chemotherapeutic that is an analog of CPT.

### **CALAA-01: siRNA for RRM2 Knockdown**

Calando's lead siRNA product candidate, CALAA-01, is a formulation containing Calando's proprietary delivery technology with an siRNA duplex payload targeting the M2 subunit of ribonucleotide reductase, a well-established cancer target. Ribonucleotide reductase catalyzes the conversion of ribonucleosides to deoxyribonucleosides and is necessary for DNA synthesis and replication. The duplex, developed at Calando, demonstrates potent anti-proliferative activity across multiple types of cancer cells. Calando believes that CALAA-01 is the first systemically delivered siRNA therapeutic to enter the oncology clinic. Calando believes that CALAA-01 is also the first clinical stage siRNA therapeutic utilizing a targeted nanoparticle delivery system.

Calando and its collaborators have generated preclinical data that demonstrate sequence-specific inhibition of tumors from the systemic administration of targeted formulations of siRNA. Using the RONDEL delivery system and siRNA developed at Calando targeting the M2 subunit of ribonucleotide reductase (RRM2), in collaboration with colleagues at the Livingston Research Institute, reduced tumor growth rates and/or tumor reduction have been observed in a variety of animal cancer models.

In May 2008, Calando initiated an open label, dose escalation phase I study in patients with solid tumors refractory to other therapies. This study is ongoing at UCLA Jonsson Cancer Center in Los Angeles, CA and at South Texas Accelerated Research Therapeutics (START) in San Antonio, Texas.

### **Product Pre-Clinical Development Programs**

#### **CALAA-02: RONDEL+siRNA**

Calando's next anti-cancer siRNA therapeutic is currently in preclinical development. The intracellular target for CALAA-02 is HIF-2alpha, or Hypoxia Inducible Factor-2 alpha. HIF-2alpha is over expressed in a number of solid tumors and is critical for many aspects of tumorigenesis, such as metastasis, angiogenesis, tumor cell proliferation, and tumor response to radiation. HIF-2alpha has been difficult to target using traditional drugs but has been shown to be effectively targeted by the proprietary siRNA in CALAA-02.

### **Intellectual Property**

Calando controls an intellectual property portfolio. Patents covering linear cyclodextrin polymers for delivery of small molecule, nucleic acid and peptide drug candidates are exclusively licensed from Caltech. These patents are directed at both RONDEL and Cycloset and contain composition of matter, method of use and manufacturing process claims. Calando also owns a patent on the siRNA active ingredient in CALAA-01 and has filed a patent application to cover the siRNA active ingredient of CALAA-02. The Camptothecin component of IT-101 is off-patent. Calando has licensed patents from Alnylam relevant to siRNA therapeutics for CALAA-01 and CALAA-02. Calando has in-licensed from R&D Pharmaceuticals exclusive rights to second generation synthetic epothilones. However, the RNAi and nanoparticle drug delivery patent landscape is complex and rapidly evolving. As such, Calando may need to obtain additional patent licenses prior commercialization of its lead drug candidates.

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### **Outsourced Manufacturing and Product Supply**

Calando currently uses, and expects to continue to be dependent upon, contract manufacturers to manufacture each of its product candidates. Calando has established a quality control and quality assurance program, including a set of standard operating procedures and specifications, designed to ensure that its products are manufactured in accordance with current Good Manufacturing Procedures, or cGMPs, and other applicable domestic and foreign regulations. Additional manufacturing resources would require additional investment, and Calando may seek to enter into additional collaborative arrangements with other parties that have established manufacturing capabilities. It is likely that Calando will continue to rely on third party manufacture of its development and commercial products on a contract basis. Currently, Calando has agreements with third party vendors to furnish CALAA-01 and IT-101 drug supply for clinical studies. Calando will be dependent upon these third parties to supply products in a timely manner manufactured in compliance with cGMPs or similar standards imposed by foreign regulatory authorities where its products are tested and/or marketed.

### **Competition**

Calando is engaged in the rapidly changing business of developing treatments for human disease through the regulation of gene expression and delivery of generic and proprietary novel cancer therapies. Competition in these fields is intense as other companies are developing therapies similar to our nanoparticle drug delivery systems, and targeting patient populations that are similar to the patient populations that are targeted by Calando. A number of companies are pursuing research and development programs relating to the emerging area of cancer therapies using nanoparticle conjugates and RNA interference. A number of these companies have filed patent applications in the area of nanoparticle conjugates and RNA interference. It is difficult to predict whether any of these companies will be successful in obtaining patent protection, whether the patent protection sought will address important aspects of the technology and to what extent these companies will be successful in their RNA interference efforts. New competitors may arise and we may not be aware of all competitors in this space. A number of Calando's competitors are more established and have greater resources than Calando does. Furthermore, even if Calando is successful in developing commercial products, it is possible that competitors will achieve greater market acceptance.

In addition to irinotecan (Pfizer/Daiichi) and topotecan (GSK), which are small molecule analogs of camptothecin, other companies are developing topoisomerase I formulations with a goal of delivering a more effective and tolerable therapy than the approved Camptothecin-based products. Companies engaged in nanoparticle chemotherapeutic drug formulations at various stages of development include, Nippon Kayaku, Sonus Pharmaceuticals, Celator Pharmaceuticals, Samyang, Cell Therapeutics, PharmaEngine, Enzon, Nektar Therapeutics, Tempo Pharmaceuticals, BIND Biosciences, Hermes, NeoPharm and Alza. This list of potential competitors may not be a complete list of competing firms developing nanoparticle-based oncology products.

Systemic delivery of siRNA and other oligonucleotide therapeutics has proven critical for the success of all nucleic acid therapeutics. Naturally, multiple firms have recognized the problem of systemic siRNA delivery as a significant opportunity and other firms are developing products in this space. Companies developing siRNA delivery products include but are not limited to Alnylam, Merck, Roche, Tekmira, RXi Pharmaceuticals, PharmRX and Intradigm. Additionally, many academic groups are developing and may seek to commercialize siRNA delivery technologies.

### **Key Personnel**

James Hamilton, M.D., M.B.A. is President of Calando. Dr. Hamilton also serves as Vice President, Medical Technologies of Arrowhead Research. Dr. Mark Davis is the Company's founder and Chief Scientific Advisor. Dr. Davis is the Warren and Katharine Schlinger Professor of Chemical Engineering and Executive Officer of Chemical Engineering at the California Institute of Technology.

Calando's Board of Directors consists of R. Bruce Stewart, Executive Chairman of Arrowhead, Christopher Anzalone, CEO and director of Arrowhead, Nanotope and Leonardo, Edward W. Frykman, member of the Arrowhead Board and Mark Davis.

As of September 30 2008 and December 12, 2008, there were 11 full time employees at Calando.

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### ***Unidym, Inc.***

#### **Liquidity**

Unidym raised a total of \$14 million of equity financing in fiscal 2008. In fiscal 2008, Unidym consumed large amounts of cash to scale up the manufacture of carbon nanotubes, scale up for the production and sale of carbon nanotube based film product, acquire another nanotech company, expand its business development activities, and prepare for an initial public offering. In the first and second quarters of fiscal 2008, Unidym expanded its executive, technical and administrative staff for these activities. Unidym's cash burn increased from \$2 million in the second quarter, to \$3.6 million in the third quarter and \$4.2 million in the fourth quarter. In the fourth quarter, it became clear that Unidym would be unable to meet its fund raising goals to support its 2009 cash needs. Moreover, technical development took longer than expected. Additionally, it became evident that dramatic changes in the financial markets would not allow for an initial public offering. Starting in October 2008, several general and administrative positions were eliminated. Approximately half of Unidym's employees at the Houston, TX facility were put on unpaid leave to conserve cash. Further cuts to personnel and consolidation of facilities are planned to bring Unidym's cash needs to 75% of those in fourth quarter 2008. Despite these changes, Unidym will still need to obtain additional cash to fund its operations and obligations through fiscal 2009.

Subsequent to September 30, 2008, Unidym obtained financing from a strategic investor. The terms of the investment include a put option whereby certain material intellectual property assets could be foreclosed on unless Unidym meets certain obligations by mid 2009. Moreover, pursuant to a license between Unidym and Rice University, should Unidym become insolvent, other material intellectual property assets would revert to Rice. See Intellectual Property below.

#### **General**

Unidym is the Company's most mature nanomaterials company and provides an example of a company-building strategy that Arrowhead plans to replicate in other areas of nanotechnology. Through the acquisition of a foundational intellectual property portfolio in the manufacture and applications of carbon nanotubes (CNTs), Unidym has developed a strong technology base in CNT technology that we believe can serve as a platform for innovation and new products. Carbon nanotubes are a novel material with extraordinary electrical, thermal, and mechanical properties. Unidym has already developed world-leading high performance carbon nanotube materials manufactured by scalable processes. Unidym's product development efforts are focused on the electronics industry, where there is continuing demand for higher performance materials. Unidym is initially targeting sales of its film product to the touch panel market. Unidym has recently entered into selective intellectual property licensing arrangements to license its CNT technologies to customers or partners in markets outside Unidym's primary focus of electronics.

Unidym's product development has been focused on thin, transparent films of carbon nanotubes on a flexible substrate. The CNT based film is designed to replace the expensive, failure-prone materials currently employed by manufacturers of such devices as touch screens, flat panel displays, solar cells and solid state lighting. CNT-based film offers substantial advantages over ITO and IZO, the currently used materials, including: lower cost, improved durability, enhanced flexibility, higher yields, better readability in display applications, and simplified processing. Unidym is currently sampling its film products to the world's leading touch panel companies. Unidym is also working with leading LCD companies, including a joint development agreement with Samsung Electronics, to incorporate CNT films into their display devices. Through its various collaborations, Unidym has also fabricated prototype LCD and electrophoretic displays incorporating CNT-based films. For its initial product offering to touch panel makers, Unidym is currently evaluating the most favorable business model to pursue. In one model, Unidym would synthesize CNTs, formulate those CNTs into a coating ink, and outsource production of the films to a toll coater to produce the film. Unidym would pay for production of the films on a time and materials basis, and Unidym would directly market and sell the films to touch panel makers. Under a second model that is less capital intensive, Unidym would synthesize CNTs and CNT inks, and then ship the inks to company that would manufacture and sell films to touch panel makers.

#### **Acquisitions**

In 2005, Arrowhead saw an opportunity in carbon nanotubes and started the company that would become Unidym to address it. We believed that CNTs had the potential to significantly impact multiple large and diverse industries. At the time Unidym was launched, the CNT market was highly fragmented with key patents dispersed across multiple owners and there was no clear industry leader. Unidym has since licensed technology from a dozen universities and acquired three prominent CNT companies, including Carbon Nanotechnologies, Inc., the pioneering company in high performance CNTs, and has become a leader in the development of innovative CNT-enabled products for the electronics industry. In the process, Unidym has assembled a strong and diverse patent portfolio that we believe covers high performance CNT manufacturing and processing, as well as multiple product applications.

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Unidym was formed when NanoPolaris, a Subsidiary of Arrowhead Research Corporation, acquired the assets of an early stage company called Unidym, Inc. At the time of the acquisition, NanoPolaris had already consolidated certain intellectual property related to carbon nanomaterials. NanoPolaris purchased the assets of the former Unidym to gain access to the company's substantial expertise and intellectual property in carbon nanotube films. After its purchase of Unidym's assets in June 2006, NanoPolaris changed its name to Unidym.



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In April 2007, Unidym merged with Carbon Nanotechnologies, Inc. (CNI) of Houston, Texas, a company founded in 2000 by the late Dr. Richard Smalley of Rice University. Dr. Smalley and his collaborators won the 1996 Nobel Prize in Chemistry for their discovery of carbon fullerenes, an allotrope (or molecular form) of carbon closely related to the carbon nanotube. Dr. Smalley's pioneering work led to the development of a suite of more than 100 patents (including 54 issued US patents) owned by CNI or exclusively licensed to CNI by Rice University, as well as the development of significant development and production infrastructure for the production of CNT materials. Since its inception, CNI provided bulk CNT materials to customers and has won research grants from government agencies such as the National Institute of Science (NIST) and the State of Missouri.

In July 2008, Unidym acquired Nanoconduction, Inc., a Sunnyvale, CA company developing nano-based electronic cooling technology ( Nanoconduction ). The merger provides Unidym with access to Nanoconduction's patent portfolio, which will supplement Unidym's existing patent portfolio and provides Unidym with additional opportunities to out-license and leverage its technology. In addition, through the merger, Unidym will gain access to research facilities and equipment that will be used in Unidym's ongoing research and development activities.

Unidym accomplished the acquisition of Nanoconduction through an equity exchange, as follows. Arrowhead invested \$250,000 in Unidym through a cashless investment by issuing 114,115 shares of unregistered Common Stock to the owners of Nanoconduction. In exchange for this investment, the Company received 138,889 additional shares of Series C Preferred Stock of Unidym. As additional consideration, Unidym agreed to assume and discharge Nanoconduction's assets and liabilities. Assets included equipment and leasehold improvements with an estimated net book value of approximately \$2.9 million including intellectual property related to the use of carbon nanotubes for thermal management. Liabilities included approximately \$1.0 million of accounts payable and accrued liabilities and approximately \$1.7 million in capital equipment loans. The equipment loans are guaranteed by Unidym and secured by a lien on Nanoconduction assets. Unidym entered into a new five-year lease for the facilities currently occupied by Nanoconduction in Sunnyvale, California, with the intention of moving Unidym's existing Menlo Park operations to the Nanoconduction facility.

## **Competition**

Unidym faces competition from a number of start-ups and established companies in the industries it enters. In the electronics industry, there are a number of start-up or private companies that are focused on the application or production of nanotubes including Atomate, C-Nano, Eikos, Nantero and Southwest Nanotechnologies. More established companies with announced CNT programs include Brewer Sciences, DuPont, Honeywell, Samsung, Sumitomo and Toray. There are also potential competitors who are pursuing alternative nanotech based approaches to the markets served by Unidym, including the start-up Cambrios and large Japanese companies such as Fujitsu.

## **Production**

### *Production Carbon Nanotube Based Transparent Conductive Films*

Unidym's film production model involves in-house synthesis of a proprietary grade of CNTs, formulation of those CNTs into a coating ink, and then shipment of that ink to an outsourced coating partner or customer for deposition. To conserve cash and pursue a strategy designed to yield revenues in the short term, Unidym is exploring partnerships or outsourcing arrangements for volume manufacture and distributions of its films.

Unidym has in-house deposition or coating equipment which is used for the deposition of CNTs onto plastic or glass substrates in sample quantities. Unidym has also tested production samples from several coating subcontractors. The use of outsourced coating partners for its touch panel films would take advantage of the substantial excess capacity left in the coating industry by the decrease in demand for photographic film. Unidym expects that given the abundance of these subcontractors and the availability of cost effective subcontract capacity, there will be no need to bring production capacity in house for the near or intermediate term. However, longer term, Unidym could decide to bring such production in house if it is advantageous to the company to do so.

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### *Carbon Nanotube Production and Purification*

Unidym has developed two different processes for commercial production: High Pressure Carbon Monoxide ( HiPco or MGP1 ) and Modified Gas Phase 2 ( MGP2 ); as well as a new process, Modified Gas Phase 3 ( MGP3 ) which is in the final stages of development and qualification. By varying production conditions and post-processing techniques, Unidym is able to produce a wide variety of nanotube grades that are tailored to different markets.

Unidym is focusing its CNT production capabilities on producing electronic grade CNTs for transparent conductive film rather than volume manufacture of several grades of bulk materials. Unidym is currently exploring more cost efficient alternatives to operating its Houston facility. In addition to significant cuts to personnel in Houston, Unidym is exploring the move of its production capabilities to its facility in Sunnyvale or outsourcing the production of its CNT products to a third party. It is expected that significant cuts in personnel in Houston will be implemented in the near future.

### **Collaborations and Partnerships**

Unidym has several ongoing joint development agreements with various partners to incorporate its transparent conductive films into touch panels and displays. In 2008, several prototypes were demonstrated at industry conferences. Unidym and Samsung Electronics Co., Ltd. extended their collaboration to integrate carbon nanotube materials as the transparent conductive layer in display devices. The world's first carbon nanotube-based color active matrix electrophoretic display (EPD) e-paper was demonstrated at the Society for Information Display in May 2008 and at the International Meeting on Information Display (iMiD) at KINTEX, Ilsan, Korea in October 2008. The new color e-paper device is a 14.3" format display that uses a carbon nanotube (CNT) transparent electrode developed by Unidym. The display was one product of the ongoing joint development agreement between Unidym and Samsung. In addition, Unidym displayed a carbon nanotube based active matrix LCD made in collaboration with Silicon Display Technology, a company based in Seoul, Korea.

In March 2008, Unidym sub-licensed certain of its intellectual property to Ensysce BioSciences Inc. ( Ensysce ) whose focus is research into the medical therapeutic applications of carbon nanotubes. From March 2008 to November 2008, Ensysce was both funded and effectively controlled by a related party to Unidym who also serves as a director of Unidym. In November 2008, Unidym sold its 50 percent interest in Ensysce to the controlling shareholder for \$700,000, and will recognize a gain on the sale during the first quarter of fiscal 2009.

Unidym entered into a strategic alliance with the Battelle Memorial Institute in July 2007 to explore opportunities to leverage their respective capabilities to commercialize products incorporating carbon nanotubes. Battelle is the world's largest non-profit independent research and development organization, with 20,000 employees in more than 120 locations worldwide. In 2008, Unidym expanded this relationship to include an alliance focused on multi-functional nanocomposites for aerospace and transportation applications.

Other collaborative projects include the use of Unidym's carbon nanotubes to increase strength and flexibility, while reducing stress failures due to flight loads, in the engine cowling of an aerobatic airplane and the use of Unidym's transparent conductive film in solar cells.

### **Marketing and Sales**

Unidym expected to generate a small amount of revenue from sales of thin films in fourth quarter of fiscal 2008. That expectation was not met and Unidym has revised its projections. Revenue is expected to be generated through direct product sales and license deals into relatively consolidated industries. In the near term, Unidym does not expect to generate enough revenue to self fund its operations and growth. Unidym currently has a distribution relationship with the large Japanese trading firm, Sumitomo, for the distribution of its CNT materials in Asia. Unidym expects to use similar distributors to assist in the distribution of its CNT-based transparent conductive films.

### **Intellectual Property**

Unidym controls an intellectual property portfolio containing more than 200 foreign and domestic patents and patent applications, including more than 90 issued patents. The portfolio contains patent claims directed to fundamental carbon nanotube compositions of matter, as well as carbon nanotube synthesis, purification, dispersion and functionalization. Furthermore, the portfolio contains claims to the use of carbon nanotubes in many different application areas including fibers, electronics, composite materials, energy storage/generation, medical devices and drug delivery. Some patents are owned by Unidym but most are exclusively licensed from institutions such as Rice University, IBM, Georgia Tech, Clemson, University of Florida, SUNY, Penn State, UCLA, Duke, Rensselaer Polytechnic Institute, and Caltech. Additionally, Unidym acquired the right to sublicense U.S. Patent 5,424,054, which is the basic patent claiming single-walled nanotube compositions of matter. Unidym also exclusively licenses Tego's entire intellectual property including Siemens AG's U.S. Patent 5,739,376 and its international counterparts, for non-therapeutic fields of use.

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Unidym has exclusively licensed its portfolio to Ensysce Biosciences Inc., in the field of the therapeutics. Unidym is currently executing a plan to encourage third parties and competitors to enter non-exclusive licenses of its intellectual property outside of its core areas. To facilitate this plan, Unidym is also making options available to acquire non-exclusive licenses at a later date.

A material portion of Unidym's intellectual property portfolio is exclusively licensed from Rice University. If the sum of Unidym's debts, liabilities and other obligations is greater than all of Unidym's assets at fair valuation or if Unidym is generally not paying its debts, liabilities and other obligations as they come due; the Rice license will terminate. See Risk Factors. If Unidym is unable to raise additional cash, Unidym may lose rights to critical intellectual property.

On November 13, 2008, Unidym raised \$2 million from the sale of Series C-1 Preferred Stock to TEL Ventures (TEL). The sale of these securities was associated with Unidym's entry into a Security Agreement granting TEL a security interest in Unidym's physical and intellectual property (the Collateral; which, however, excludes Unidym's rights under the Rice license and shares of Ensysce Biosciences, Inc.). The Subscription Agreement provided TEL with two put options. TEL may exercise the first put option if Unidym fails to enter into a Joint Development Agreement with TEL by June 30, 2009. In that case, Unidym must buy back TEL's Unidym shares for \$2 million before March 2010. TEL may exercise the second option if Unidym fails to meet certain cash requirements by June 30, 2009. Those requirements would be met if Unidym raises \$7 million through any combination of a sale of its equity; the sale or license of some or all of its assets and businesses including positions in Ensysce Biosciences, Nexeon MedSystems or Nanoconduction; or sales of products. Only if TEL exercises this put option between June 30 and July 31, 2009, shall Unidym be obligated to repurchase the Series C-1 Preferred Stock for \$2.4 million within ten days notification of exercise. In the event of a default under the Security Agreement, e.g., inability to pay either of the put options, bankruptcy, admission of inability to pay its bills; TEL can take possession of the Collateral and keep net proceeds of any sale thereof. See Risk Factors. If Unidym is unable to raise additional cash, Unidym may lose rights to critical intellectual property.

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### **Key Personnel**

Mark Tilley, Ph.D is the CEO of Unidym and Vice President, Advanced Materials at Arrowhead. Dr. Tilley joined Arrowhead from a 9 year tenure at DSM N.V. a \$12B Netherlands based specialty performance materials and life science company. During his tenure, he worked in DSM's venturing arm, led marketing and technical teams, and built a nano-enabled flat panel displays materials business that was acquired by JSR in 2005. Dr. Tilley also co-founded Kriya Materials B.V., a venture capital backed nano-materials and coatings company based in the Netherlands. Dr. Tilley has held marketing and R&D positions at SDC Coatings, a J.V. founded by Dow Corning and Pilkington Glass, Valspar and GE Plastics where he started his career at their Corporate R&D center as a Senior Scientist. He holds a BS in Chemistry from the University of Manchester Institute of Science and Technology in Manchester, UK, a PhD from North Dakota State University in Fargo, and a MBA from Pepperdine University.

Unidym's Board of Directors is comprised of R. Bruce Stewart, Executive Chairman of Arrowhead, Christopher Anzalone, CEO and director of each Arrowhead, Nanotope and Leonardo, Edward W. Frykman and Charles McKenney, both Arrowhead Directors, Dr. Bob Gower, former CEO of CNI, and Ray McLaughlin, former CFO of CNI.

At September 30, 2008, Unidym had 44 full-time employees. Subsequent to September 30, 2008, Unidym has streamlined its general and administrative staff, including its CFO and financial staff in light of the current state of the financial markets. On December 14, 2008, the employment of Unidym's CEO was terminated. Unidym is expecting to make further cuts in its production and research staffs. On December 15, 2008, Unidym had 33 full time employees, 7 of which were on unpaid leave as a cash conservation measure.

### ***Agonn Systems, Inc.***

#### **General**

Arrowhead founded Agonn in May 2008 to explore, develop and commercialize nanotechnology-based energy storage devices for electric vehicles and other large format applications. Agonn is pursuing a strategy to acquire energy storage technologies based on nanoscale engineering from research institutions. Agonn has outsourced the development of prototype ultracapacitors based on carbon nanomaterials and other advanced materials. We believe the markets for energy storage products are substantial, ranging from consumer electronics to vehicles to heavy industry. We believe that emerging clean technology platforms offer market opportunities for new energy storage devices, in part because traditional batteries lack sufficient performance for widespread adoption.

Ultracapacitors are energy storage devices that generally have high power but low energy storage capabilities. In other words, they can provide large bursts of power, but only for short periods of time. However, unlike batteries which generally take minutes or hours to charge, ultracapacitors can be charged in seconds or less. Moreover, while the lifetimes of the best lithium ion batteries are generally limited to several thousand charging cycles, ultracapacitors can last for hundreds of thousands of cycles. Given these characteristics, ultracapacitors often serve as complements to, as opposed to replacements, for batteries. If the energy storage capability of ultracapacitors could be sufficiently increased, however, ultracapacitors could represent a viable alternative to batteries in certain applications. This could result in ultracapacitor-based energy storage devices that are rapidly chargeable, capable of delivering large amounts of power over long periods of time, while also being lighter and more long-lived than currently available batteries.

#### **Research and Development**

Agonn is currently pursuing a capital efficient R&D model based on outsourced prototyping and testing. Agonn is prototyping and testing different electrode architectures based on carbon nanomaterials (including random networks of carbon nanotubes, vertically aligned carbon nanotubes, and graphene) as well as metal nitride nanoparticles. Additionally, Agonn is evaluating novel electrolytes that have been shown to operate at higher voltages than existing electrolytes and within greater temperature ranges. Agonn is also evaluating new cell designs based on asymmetric electrode configurations. Concurrent with its technology evaluation program, Agonn is seeking to determine the most cost effective path for large volume manufacturing of ultracapacitor products based on these new materials. These activities are preparatory in nature and require little capital and other resources. If Agonn is able to aggregate a suite of intellectual property relating to the field of ultracapacitor technology, based on cash resources, technology development and market opportunity, Arrowhead may more aggressively pursue the development of Agonn.

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### **Intellectual Property**

Through its outsourced prototyping, Agonn is in the process of generating new intellectual property and identifying key intellectual property for potential future acquisition.

### **Key Personnel**

John Miller is the President of Agonn. Mr. Miller is also Vice President, Business Development at Arrowhead.

Agonn's board of directors consists of John Miller, Christopher Anzalone, CEO and Director of each Arrowhead, Nanotope and Leonardo, and Mark Tilley, Arrowhead's Vice President, Advanced Materials and CEO of Unidym.

At September 30, 2008, Agonn had no facilities or employees and is managed entirely by Arrowhead.

### ***Tego BioSciences Corporation***

#### **General**

Tego was formed to acquire the assets of C-Sixty, Inc. in April 2007. Since 1999, C-Sixty had been developing fullerene based products. C-Sixty's primary asset was an intellectual property portfolio which includes key patents for the modification of fullerenes. Fullerenes are a family of symmetrical carbon-cage molecules whose prototypical soccer-ball shaped member is comprised of sixty carbon atoms (denoted C60).

In order to exploit the therapeutic potential of fullerenes, they must first be chemically modified to render them water-soluble. A patented process known as the Bingel reaction is of particular significance to fullerene chemistry because it enables modification of the fullerene sphere to provide solubility and appropriate physiologic behavior. Tego has an exclusive license to patents directed at the Bingel reaction itself, as well as a large number of modified soluble fullerenes created through its use. Tego also owns or has exclusive licenses to patents directed to a variety of medical uses of Bingel-modified fullerenes.

Tego does not initially intend to manufacture and market its products directly. Rather, it is pursuing a strategy of partnering, licensing, and outsourced manufacturing.

#### **Collaborations, Research and Development**

Tego does not intend to hire staff to develop fullerene products. However, Tego is currently evaluating certain proprietary fullerenes for their suitability as potential therapeutics in macular degeneration utilizing a contract research organization.

The National Cancer Institute, working in concert with the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA), established the Nanotechnology Characterization Laboratory ([ncl.cancer.gov](http://ncl.cancer.gov)) to perform preclinical efficacy and toxicity testing of nanoparticles. In August 2008, the NCL issued a report containing the evaluation of several Tego owned fullerenes entitled,

Functionalized Fullerenes for C-Sixty, Inc. which is available on the NCL's website at the following link:

[http://ncl.cancer.gov/NCL200701A\\_073007.pdf](http://ncl.cancer.gov/NCL200701A_073007.pdf)

Tego and the Huntington Medical Research Institute (HMRI) have completed a project investigating the hyperpolarization potential of the <sup>13</sup>C-labeled fullerene derivatives developed by Tego. The study found that a proprietary carbon-13 labeled fullerene provided a sufficiently strong signal to potentially enable powerful real time magnetic resonance imaging of biological and physiological functions in patients.

To conserve cash, Tego is pursuing a model that seeks to earn revenue from licenses and collaborative partnerships. To the extent cash resources permit, Tego will focus any future development efforts on contrast agents and therapeutics for back of the eye disease.

#### **Competition**

Tego is competing with other companies developing fullerene products as well as alternatives to fullerene products. There are several companies that manufacture and sell fullerenes and fullerene formulations, including Frontier Carbon Corporation (Mitsubishi subsidiary) and Nano-C. There are also companies developing fullerene-based therapeutics, including Luna nanoWorks and Vitamin C60 Bioresearch (Mitsubishi)

subsidiary).

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### **Intellectual Property**

Tego controls a domestic and international patent portfolio. It owns and controls patents covering a library of functionalized fullerenes as well as methods of their synthesis. The fullerenes on which Tego has concentrated its efforts are C3 and DF1. Tego is the exclusive licensee of Siemens AG's U.S. Patent 5,739,376 and its international counterparts for therapeutics and diagnostics. The Bingel patent covers a vast library of fullerenes functionalized according to the Bingel method, e.g., C3, as well as methods of making them. Tego also exclusively licenses Siemens U.S. Patent No. 6,506,928 and its international counterparts for therapeutics and diagnostics. This patent covers dendrimeric fullerenes such as DF1. Tego licenses patents from Washington University which are directed at methods of using Tego's fullerenes, e.g., C3, to enhance neuronal survival in a variety of contexts. Tego further owns patents and applications related to the use of substituted fullerenes in drug delivery, as contrast agents; as well as for treating dermatological conditions, oxidative stress, shock and hearing loss.

### **Key Personnel**

Dr. Thomas Haag is Chief Executive Officer of Tego. Dr. Haag also serves as General Counsel and Chief Patent Officer of Arrowhead and Corporate Secretary and Counsel to Unidym, Inc. Prior to joining Arrowhead, Dr. Haag was in private practice in the Washington D.C. offices of Kenyon & Kenyon LLP and McDermott Will & Emery LLP. Dr. Haag received his B.S. in Biology and Ph.D. in Molecular, Cell & Developmental Biology from UCLA where he was an NIH Predoctoral Fellow in Genetic Mechanisms. He graduated from The George Washington University Law School with honors, receiving the ABA/BNA Award for Excellence in the Study of Intellectual Property Law.

Tego's Board of Directors is composed of R. Bruce Stewart, Executive Chairman of Arrowhead, Christopher Anzalone, CEO and director of each Arrowhead, Nanotope & Leonardo, Edward W. Frykman, an Arrowhead Board member and John Miller.

As of September 30, 2008, Tego has had no employees or facilities and is managed entirely by Arrowhead.

### **Minority Investments**

#### ***Nanotope, Inc.***

#### **General**

Nanotope is a company in the field of regenerative medicine developing a suite of products customized to regenerate specific tissues; including neuronal, vascular, bone, myocardial, and cartilage. Its two lead candidates are focused on spinal cord regeneration and treatment of peripheral artery disease (PAD). PAD causes the loss of vasculature in the extremities and it has been estimated that as many as 20% of people over the age of 70 has some form of PAD. Currently there is no treatment for regenerating lost vasculature. Nanotope has demonstrated in multiple animal models that injection of its angiogenic compound leads to revascularization of affected areas. Importantly, neither the spinal cord or PAD treatments use stem cells. Nanotope's products work with surviving cells and tissues to spur regeneration.

The Company acquired its initial stake in Nanotope from a Nanotope shareholder in April 2008 and increased its position through a direct investment of \$2M in two tranches of \$1 million each in July and September 2008. At September 30, 2008, the Company owned 22% of Nanotope's outstanding securities. The Company is interested in increasing its stake in Nanotope if the opportunity arises, the Company has the capital resources and Nanotope's technology development continues to move forward.

#### **Related Party Interests**

Nanotope was co-founded by the Company's President and Chief Executive Officer, Dr. Christopher Anzalone, through the Benet Group, a private investment entity solely owned and managed by Dr. Anzalone. Through the Benet Group Dr. Anzalone owns 1,395,900 shares of Nanotope common stock, or approximately 14.2% (after giving effect to the sale of stock to Arrowhead in its investments in Nanotope) of Nanotope's outstanding voting securities. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Nanotope directly or through the Benet Group. The Benet Group has the right to appoint a representative to the board of directors of Nanotope. Dr. Anzalone currently serves on the Nanotope board in a seat reserved for Nanotope's CEO and another individual holds the seat designated by the Benet Group. Dr. Anzalone has served as President and Chief Executive Officer of Nanotope since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Nanotope since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Nanotope before he joined the Company.

#### ***Leonardo Biosystems, Inc.***

**General**

Leonardo is a drug delivery company that employs a novel strategy aimed at dramatically increasing targeting efficiency. The Company currently owns 6% of Leonardo. Leonardo's silicon microparticulate 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. Animal testing suggests that Leonardo's platform enables significantly increased targeting. The Company is interested in increasing its stake in Leonardo if the opportunity arises, the Company has the capital resources and Leonardo's technology development continues to move forward.

**Related Party Interests**

Like Nanotope, Leonardo was co-founded by the Company's President and Chief Executive Officer, Dr. Christopher Anzalone, through the Benet Group, a private investment entity solely owned and managed by Dr. Anzalone. Through the Benet Group Dr. Anzalone owns 918,750 shares of Leonardo common stock, or approximately 17% of the outstanding stock of Leonardo. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Leonardo directly or through the Benet Group. The Benet Group has the right to appoint a representative to the board of directors of Leonardo. Dr. Anzalone currently serves on the Leonardo board in a seat reserved for Leonardo's CEO and another individual holds the seat designated by the Benet Group. Dr. Anzalone has served as President and Chief Executive Officer of Leonardo since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Leonardo since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Leonardo before he joined the Company.



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### ***Aonex Technologies, Inc.***

In May 2008, Arrowhead sold its majority-owned subsidiary Aonex Technologies, Inc. to New Hampshire-based AmberWave Systems, Inc. for an upfront fee of \$450,000 and earn-out payments of up to \$7.95 million plus a royalty on solar products or licenses covering 10 years from the date of the merger. AmberWave took over Aonex's Pasadena, California operations and is continuing to develop Aonex's technology. The losses incurred by Aonex are segregated in the Consolidated Statement of Operations as Loss from Operation of Discontinued Aonex.

### **Academic Partnerships**

Since inception, Arrowhead has worked with some of the most outstanding academic institutions in the country, including the California Institute of Technology (Caltech), Stanford University, Duke University and the University of Florida, in critical areas such as stem cell research, carbon electronics and molecular diagnostics. This has provided the Company with deep network in the academic community, insight into cutting edge technologies and a world class scientific advisory board. Through these partnerships, Arrowhead has gained access to exclusive rights that have formed the basis for the Company's subsidiaries and minority investments and have leveraged university resources to further develop and test technology in a highly cost effective way. The collaborations with academic scientists have included technology licenses and options to license technology, sponsored research, donations to the labs of individual scientists and use of university facilities that are made available to development stage companies. In prior years, Arrowhead devoted significant capital resources to sponsored research. As the Subsidiaries have matured, the Company has decreased its reliance on sponsored research for technology development and sponsored research expense has decreased. As of September 30, 2008, Arrowhead had one active sponsored research agreement at Duke University through Unidym. Depending on capital resources, Arrowhead is likely to continue to invest in nanoscience research and development through sponsored research agreements at universities.

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**ITEM 1A. RISK FACTORS**

*We are a development stage company and we have limited historical operations. 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.*

*The following is a summary of certain risks we face. They are not the only risks we face. Additional risks of which we are not presently aware or that we currently believe are immaterial may also harm our business and results of operations. The trading price of our common stock could decline due to the occurrence of any of these risks, and investors could lose all or part of their investment. In assessing these risks, investors should also refer to the other information contained or incorporated by reference in our other filings with the Securities and Exchange Commission.*

**Risks Related to Our Financial Condition**

*We do not have sufficient cash reserves to fund our activities at their current pace for the next fiscal year.*

Our plan of operations is to provide substantial amounts of research project funding and financial support for majority-owned Subsidiaries over an extended period of time. Our Board of Directors has adopted a cash conservation strategy that scales back Arrowhead's financial support for Unidym and Calando at this time. This has influenced Unidym's shift from capital intensive bulk CNT manufacturing to thin film license and partnerships for electronic ink products. Development of new drug candidates at Calando has slowed during this time as well. We will need to obtain additional capital in the near term to support all of these projects, and we may plan to do so by out-licensing technology, selling one or more of our Subsidiaries, securing funded partnerships, conducting one or more private placements of equity securities of Arrowhead or its subsidiaries, selling additional securities in a registered public offering, or through a combination of one or more of such financing alternatives. However, there can be no assurance that we will be successful in any of these endeavors or, if we are successful that such transactions will be accomplished on favorable terms. If we are unable to obtain additional capital, we will be required to engage in additional cash savings by limiting further activities at one or more of our Subsidiaries, or at Arrowhead, which could materially harm our business and our ability to achieve cash flow in the future, including possibly delaying or reducing implementation of certain aspects of our plan of operations or deferring or abandoning research programs. Even if we are successful in raising capital for one area of our business, because Arrowhead and each Subsidiary are separate entities, it could be difficult or impossible to allocate funds as we would like.

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

Neither Arrowhead nor its Subsidiaries generate substantial revenue, and, to date, our operations, research and development activities have been funded through the sale of Arrowhead securities and securities of our subsidiaries. Current market conditions could impair our ability to raise the capital we need and if we are unable to secure additional cash resources from the sale of securities or other sources, it could become necessary to slow, interrupt or close down development efforts at Calando or Unidym. In addition, we may have to cut expenses at the Arrowhead level which could impair our ability to manage our business and our Subsidiaries. Even if investment capital is available to us, in the current market, the terms may be onerous and could significantly dilute our ownership interest in either Calando or Unidym. The sale of additional Arrowhead stock to fund operations could result in significant dilution to stockholders.

The strategy for eventual monetization of our Subsidiaries could depend on our ability to exit our ownership position each Subsidiary. Exit opportunities could include an initial public offering for the Subsidiary or acquisition of the Subsidiary by another company. Due to the current financial crisis, companies are adopting conservative acquisition strategies and, even if there is interest, may not be able to acquire our Subsidiaries on attractive terms or at all. This could reduce the return we realize on our investment if we sell a Subsidiary. Additionally, the market for initial public offerings is severely limited, which limits public exit opportunities for our Subsidiaries.

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***Our Subsidiaries have entered into 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 have entered into exclusive, long-term license agreements with Rice University, California Institute of Technology (Caltech), 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 related to the commercialization of the licensed technology. We cannot give any assurance that we will 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. Failure by us to satisfy our obligations under these agreements may result in the modification of the terms of the licenses, such as by rendering them 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.

***If Unidym is unable to raise additional cash, Unidym may lose rights to critical intellectual property.***

There is also the possibility that Unidym investor TEL Ventures will have the right to exercise a put right in July 2009, forcing Unidym to redeem TEL Venture's Series C-1 Preferred Stock for \$2.4 million. Unidym's potential repurchase obligation is secured by a first priority lien in Unidym's physical and intellectual property (excluding rights under the Rice license). In the event Unidym is unable to pay TEL Ventures upon exercise of the put right, TEL Ventures will acquire all right, title and interest in the collateral intellectual property and Unidym's patent protection for its products and its ability to pursue a licensing strategy would be impaired significantly.

Further, Unidym is required to meet certain financial covenants pursuant to the Rice University license agreement it acquired upon its acquisition of CNI. When Unidym acquired CNI, CNI possessed intellectual property rights concerning carbon nanotubes that it had licensed from Rice University. The Rice license includes financial covenants tested quarterly for compliance. If Unidym fails to meet the financial covenants, the Rice license automatically terminates. If this should happen, the value of Unidym's intellectual property portfolio would be significantly and adversely affected and Unidym would likely lose patent protection for its products and licensing opportunities for the majority of its CNT intellectual portfolio.

***We have debt on our balance sheet, which could have consequences if we were unable to repay the principal or interest due.***

**Calando.** Calando has \$2.7 million in unsecured convertible promissory notes outstanding of which \$1.1 m has been received. The notes bear 10% interest accrued annually and have a two year maturity. Following maturity, the notes become payable on demand. If Calando is unable to meet its obligations to the bearers of the notes after maturity, Arrowhead may also not be in a position to lend Calando sufficient cash to pay such demand notes individually or all at once. Unless other sources of financing become available, this could result in Calando's insolvency and Calando would be unable to continue operations.

**Unidym.** We have debt on our consolidated balance sheet, including a capital lease obligation acquired in connection with Unidym's acquisition of Nanoconduction, Inc. The capital lease obligation requires us to pay \$1.5 million in 19 monthly payments for capital equipment at Unidym's Sunnyvale, California location and the equipment itself serves as collateral for the debt. Unidym's ability to make payments on its indebtedness will depend on its ability to conserve the cash that it has on hand and to generate cash in the future. Neither Unidym nor Arrowhead currently generates significant revenue. Because Unidym does not currently have a substantial amount of cash on hand, Unidym might be required to divert cash from development activities or to generate cash via debt or equity financing to be able to meet the monthly payment requirements under the capital lease obligation. This, to some extent, is subject to general economic, financial, competitive, legislative, regulatory and other factors that are beyond our control. Also, given the current economic credit crisis, financing options might be limited going forward, which could prevent Unidym from obtaining the necessary funds to pay its indebtedness when due. Because the equipment serves as collateral for the debt, if Unidym is unable to make the monthly payments when due, the lessor of the equipment, at its discretion, may seize the equipment and Unidym would not be able to use the equipment in its development activities.

***The costs to fund the operations of our Subsidiaries are difficult to predict, and our anticipated expenditures in support of our Subsidiaries may increase for a variety of reasons.***

It is possible that the completion of our clinical studies could be delayed for a variety of reasons, including difficulties in enrolling patients, delays in manufacturing, incomplete or inconsistent data from the pre-clinical or clinical trials, and difficulties evaluating the trial results. Any delay in completion of a trial would increase the cost of that trial, which would harm the Company's results of operations. Due to these uncertainties, the Company cannot reasonably estimate the size, nature or timing of the costs to complete or the amount or timing of the net cash inflows from the current activities of any of our biopharmaceutical Subsidiaries or investments. Until the Company obtains further relevant pre-clinical and clinical data, it will not be able to estimate its future expenses related to these programs or when, if ever, and to what extent, the

Company will receive cash inflows from resulting products.

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Development, manufacturing and sale of cost effective electronic products incorporating carbon nanotubes may require significant additional investment and take a long time. It is possible that the development and scale up of Unidym's carbon nanotube manufacturing effort and its development and scale up of its transparent conductive film products could be delayed for a number of reasons, including unforeseen difficulties with the technology development and delays in adoption of the technology by customers. Any delay would result in additional unforeseen costs, which would harm the Company's results of operations. Due to these uncertainties, the Company cannot reasonably estimate the size, nature or timing of the costs to complete the development of Unidym's products or net cash inflows from Unidym's current activities.

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### **Risks Related to Our Business Model and Company**

*We are a development stage company and our success is subject to the substantial risks inherent in the establishment of a new business venture.*

The implementation of our business strategy is still in the development stage. We currently own majority interests in four subsidiary companies, investments in two early stage biotech companies and, through Unidym, one university research project at Duke University. Our business and operations should be considered to be in the development stage and subject to all of the risks inherent in the establishment of a new business venture. Accordingly, our intended business and operations may not prove to be successful in the near future, if at all. Any future success that we might enjoy will depend upon many factors, several of which may be beyond our control, or which cannot be predicted at this time, and which could have a material adverse effect upon our financial condition, business prospects and operations and the value of an investment in our company.

*The costs and effect of consolidating Unidym's facilities and operations are difficult to predict and could be substantial.*

Unidym is in the process of consolidating its facilities and operations. Unidym has leased a new facility in Texas that it has decided not to occupy and we cannot predict how long it will take to sublease the property, if it can be subleased at all. The lease on a portion of Unidym's current facility has been terminated and the facility must be completely vacated in the near future. As part of its lease on its Houston facility, Unidym is obligated to make certain repairs and clean up the facility. In addition, Unidym has two facilities in Northern California, both of which it will continue to occupy until its Sunnyvale, CA facility is retrofitted with all of the capabilities that are needed. The amount of time for which Unidym will be obligated under the various leases and the cost for retrofitting is difficult to estimate, as well as the associated costs. These costs will divert funds from development activities and could place significant financial strain on Unidym and the time required to make the retrofits could result in delay in bringing Unidym's products to market. The consolidation included some recent reduction in Unidym's management and technical teams and Unidym plans to make additional cuts in the near future. With these cuts, it is possible that valuable know-how will be lost and that Unidym's development efforts could be negatively affected.

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

Our company finances research and development of nanotechnology, which is a new and unproven field. Our research scientists are working on developing technology in various stages. However, such technology's commercial feasibility and acceptance is unknown. Scientific research and development requires significant amounts of capital and takes an extremely 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. For example, our scientists must determine how to design and develop nanotechnology applications for potential products designed by third parties for use in cost-effective manufacturing processes. Because of these uncertainties, it is possible that none of our potential applications will be successfully developed. If we are unable to successfully develop nanotechnology applications for commercial use, we will be unable to generate revenue or build a sustainable or profitable business.

*We have not generated significant revenues and our business model does not predict significant revenues in the foreseeable future.*

To date, we have only generated a small amount of revenue as a result of our current plan of operations. Moreover, given our strategy of financing new and unproven technology research, we do not expect to realize significant revenue from operations in the foreseeable future, if at all.

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

Even if our research and development yields technologically feasible applications, we may not successfully develop commercial products, and even if we do, we may not do so on a timely basis. If our research efforts are successful on the technology side, it could take at least several years before this technology will be commercially viable. During this period, superior competitive technologies may be introduced or customer needs may change, which will diminish or extinguish the commercial uses for our applications. Because nanotechnology is an emerging field, the degree to which potential consumers will adopt nanotechnology-enabled products is uncertain. We cannot predict when significant commercial market acceptance for nanotechnology-enabled products will develop, if at all, and we cannot reliably estimate the projected size of any such potential market. If markets fail to accept nanotechnology-enabled products, we may not be able to generate revenues from the commercial application of our technologies. 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

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acceptance of our technology among original equipment manufacturers and customers, or if the associated products do not achieve wide market acceptance, our business will be materially and adversely affected.

***We may be unable to scale up our manufacturing processes in a cost effective way.***

In some cases, nanotechnology will require new technological and manufacturing processes that, at this time, are very expensive and subject to error. There is no assurance that technology and manufacturing processes will expand and improve quickly enough to enable our targeted products to be made within rigorous tolerances cost effectively. If manufacturing and mass production are not available at a favorable cost, our technology may not be adopted by the applicable industry. Under such scenario, we may not achieve our business plan for one or more process or product, which could adversely impact the value of our common stock.

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*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 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, 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 attendant 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 risks could impair our ability to generate revenues and harm our business and financial condition.

*Arrowhead will need to retain a controlling interest, by ownership, contract or otherwise, in Calando and Unidym in order to avoid being deemed an investment company under the Investment Company Act of 1940.*

Companies that have more than 100 U.S. shareholders or are publicly traded in the U.S. or are, or hold themselves out as being, engaged primarily in the business of investing, reinvesting or trading in securities are subject to regulation under the Investment Company Act of 1940. Unless a substantial part of Arrowhead's assets consists of, and a substantial part of Arrowhead's income is derived from, interests in majority-owned subsidiaries and companies that it primarily controls, whether by contract or otherwise, Arrowhead may be required to register and become subject to regulation under the Investment Company Act. Because Investment Company Act regulation is, for the most part, inconsistent with Arrowhead's strategy of actively managing and operating its portfolio companies, a requirement to operate its business as a registered investment company would restrict our operations and require additional resources for compliance.

If Arrowhead is deemed to be, and is required to register as, an investment company, it will be forced to comply with substantive requirements under the Investment Company Act, including:

limitations on its ability to borrow;

limitations on its capital structure;

restrictions on acquisitions of interests in associated companies;

prohibitions on transactions with affiliates;

restrictions on specific investments; and



compliance with reporting, record keeping, voting, proxy disclosure and other rules and regulations.

***Nanotechnology-enabled products are new and may be viewed as being harmful to human health or the environment.***

There is public concern regarding the human health, environmental and ethical implications of nanotechnology that could impede market acceptance of products developed through these means. Nanotechnology-enabled products could be composed of materials such as carbon, silicon, silicon carbide, germanium, gallium arsenide, gallium nitride, cadmium selenide or indium phosphide, which may prove to be unsafe or harmful human health or to the environment because of the size, shape or composition of the nanostructures. For this reason, these nanostructures may prove to present risks to human health or the environment that are different from and greater than the better understood risks that may be presented by the constituent materials in non-nanoscale forms. Because of the potential, but at this point unknown, risks associated with certain nanomaterials, government authorities in the United States or individual states, and foreign government authorities could, for social or other purposes, prohibit or regulate the use of some or all nanotechnologies. The United States Environmental Protection Agency has in that regard recently taken steps towards regulation of the manufacture and use of certain nanotechnology-enabled materials, including those containing carbon nanotubes or nanosilver. Further, in a just-released report, the United States National Academy of Sciences/National Research Council concluded that the U.S. government needs to develop a more robust and coordinated plan for addressing the potential environmental, health, and safety risks of nanomaterials. The regulation and limitation of the kinds of materials used in or used to develop nanotechnology-enabled products, or the regulation of the products themselves, could halt or delay the commercialization of nanotechnology-enabled products or substantially increase the cost, which will impair our ability to achieve revenue from the license of nanotechnology applications.

***We may not be able to effectively secure first-tier research and development projects when competing against other ventures.***

We compete with a substantial number of other companies that fund early-stage, scientific research at universities to secure rights to promising technologies. In addition, and many venture capital firms and other institutional investors invest in companies seeking to commercialize various types of emerging technologies. Many of these companies have greater resources than we do. Therefore, we may not be able to secure the opportunity to finance first-tier research and commercialization projects. 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, including the manufacture of Calando's product candidates. 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. In addition, due to the recent tightening of global credit and the disruption in the financial markets, there may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators. 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 business ventures to succeed.***

Our model to integrate and oversee the strategic direction of various subsidiaries and 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.

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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 our company could decline.

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

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.

***Failure to effectively manage our growth could place strains on our managerial, operational and financial resources and could adversely affect our business and operating results.***

Arrowhead provides managerial and operational support for our Subsidiaries. At times over the course of the Company's development, our growth has placed, and is expected to continue to place, a strain on our managerial, operational and financial resources. Further, as our subsidiaries' businesses grow, we will be required to manage multiple relationships. Any further growth by us or our subsidiaries, or an increase in the number of our strategic relationships will increase this strain on our managerial, operational and financial resources. This strain may inhibit our ability to achieve the rapid execution necessary to implement our business plan, and could have a material adverse effect upon our financial condition, business prospects and operations and the value of an investment in our company. In the near term, Arrowhead has consolidated management responsibilities for our Subsidiaries at the Arrowhead level. Failure to effectively manage those responsibilities in light of increased responsibilities and the Company's financial condition could have a material adverse effect upon the value of the Company.

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

Our future success will depend to a significant extent on the continued services of our key employees. In addition, we rely on several key executives to manage each of our subsidiaries. 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, sales, marketing and additional managerial personnel. 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 CEO and President is a minority equity holder in and the founder, CEO and board member of Nanotope and Leonardo. 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 will have a greater influence on such decisions.

***Our research and product development efforts pertaining to the pharmaceutical industry are subject to additional risks.***

Our subsidiaries, Calando and Tego, as well as minority investments Nanotope and LBS, are focused on research and development projects related to new and improved pharmaceutical candidates. Drug development is time-consuming, expensive and risky. Even product candidates that appear promising in the early phases of development, such as in early animal and human clinical trials, often fail to reach the market for a number of reasons, such as:

clinical trial results are not acceptable, even though preclinical trial results were promising;

inefficacy and/or harmful side effects in humans or animals;

the necessary regulatory bodies, such as the FDA, did not approve our potential product for the intended use; and

manufacturing and distribution is uneconomical.

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. If Calando is unable to cost-effectively achieve acceptance of their respective biopharmaceutical technology, or if the associated drug products do not achieve wide market acceptance, the business of Calando will be materially and adversely affected, and the value of our interest in this subsidiary will diminish.

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***Any drugs developed by our Subsidiaries may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.***

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the United States healthcare system have been introduced or proposed in Congress and in some state legislatures, including reductions in the cost of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

The ability of Calando, Tego and our minority investments Nanotope and LBS to market products successfully will depend in part on the extent to which third-party payers are willing to reimburse patients for the costs of their products and related treatments. These third-party payers include government authorities, private health insurers and other organizations, such as health maintenance organizations. Third party payers are increasingly challenging the prices charged for medical products and services. In addition, the trend toward managed healthcare and government insurance programs could result in lower prices and reduced demand for the products of these companies. Cost containment measures instituted by healthcare providers and any general healthcare reform could affect their ability to sell products and may have a material adverse effect on them, thereby diminishing the value of the Company's interest in these Subsidiaries. We cannot predict the effect of future legislation or regulation concerning the healthcare industry and third party coverage and reimbursement on our business.

***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 Minority Interests were the result of negotiation with Subsidiary management and equity holders, and the investment valuations were not 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 there exist comparable public companies to provide a meaningful valuation comparison. Accordingly, we have not 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 lower or higher 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.***

Our subsidiaries have licensed rights to pending patents and have filed and will continue to file patent applications. The 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. 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.

***Our ability to develop and commercialize products will depend on our ability to enforce our intellectual property rights and operate without infringing the proprietary rights of third parties.***

Our ability and the ability of our subsidiaries to develop and commercialize products based on their respective patent portfolios, will depend, in part, on our ability and the ability of our subsidiaries to enforce those patents and operate without infringing the proprietary rights of third parties. There can be no assurance that any patents that may issue from patent applications owned or licensed by us or any of our subsidiaries will provide sufficient protection to conduct our respective businesses as presently conducted or as proposed to be conducted, or that we or our subsidiaries will remain free from infringement claims by third parties.

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

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Because the nanotechnology intellectual property landscape 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

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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 or our subsidiaries, 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. There can also be no assurance 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.

***The technology licensed by our Subsidiaries from various third parties may be subject to government rights and retained rights of the originating research institutions.***

We license technology from Caltech, Rice University, 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 collaborators 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 collaborators 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.

### **Risks Related to Regulation of Our Products**

***We will need approval from governmental authorities in the United States and other countries to successfully realize commercial value from our activities.***

In order to clinically test, manufacture and market products for commercial use, two of our current subsidiaries and both of our investments must satisfy mandatory procedures and safety and effectiveness standards established by various regulatory bodies, including the U.S. Food and Drug Administration, or FDA. Technology and product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources. The time and expense required to perform the necessary testing can vary and is substantial. In addition, no action can be taken to market any biologic, drug or device in the United States until the FDA approves an appropriate marketing application. Furthermore, even after initial FDA approval has been obtained, further trials may be required to obtain additional data on safety and effectiveness. Adverse events that are reported during regulatory trials or after marketing approval can result in additional limitations being placed on a product's use and, potentially, withdrawal of the product from the market. Any adverse event, either before or after approval, can result in product liability claims against us, which could significantly and adversely impact the value of our common stock.

***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 assure you that our 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.

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In order to avoid regulation under the Investment Company Act, Arrowhead may choose to make additional pro rata investments in Unidym to maintain a controlling interest.

*If export controls affecting our products are expanded, our business will be adversely affected.*

The U.S. government regulates the sale and shipment of numerous technologies by U.S. companies to foreign countries. Our subsidiaries may develop products that might be useful for military and antiterrorism activities. Accordingly, U.S. government export regulations could restrict sales of these products in other countries. If the U.S. government places burdensome export controls on our technology or products, our business would be materially and adversely affected. If the U.S. government determines that we have not complied with the applicable export regulations, we may face penalties in the form of fines or other punishment.

## **Risks Related to our Stock**

*Stockholder equity interest may be substantially diluted in additional financings.*

Our certificate of incorporation authorizes the issuance of 70,000,000 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. As of September 30, 2008, 42,934,517 shares of common stock and no shares of preferred stock were issued and outstanding. As of September 30, 2008, 1,559,000 shares and 4,738,310 shares were reserved for issuance upon exercise of options granted under our 2000 Stock Option Plan, or 2000 Plan, and 2004 Equity Incentive Plan, or 2004 Plan, respectively. As of September 30, 2008, options to purchase 1,559,000 shares were outstanding under our 2000 Plan and options to purchase 4,710,322 shares were outstanding under our 2004 Plan. In addition, an inducement grant of an option to purchase 2,000,000 shares of common stock was issued to our CEO as part of his compensation package. As of September 30, 2008, we had warrants outstanding to purchase 5,973,851 shares of common stock that are callable by us under certain market conditions. The issuance of additional securities in financing transactions by us or through the exercise of options or warrants would 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 during fiscal 2005, 2006, 2007, and 2008 and may continue to do so in the future.*

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 do not expect to generate substantial revenue from the license or sale of our nanotechnology 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;

developments in our strategic relationships with scientists within the nanotechnology field;

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 nanotechnology as the next technological wave;

announcements regarding developments in the nanotechnology field in general;

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

quarterly 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 any extreme fluctuations in the market price of our common stock could result in the loss of all or part of your investment.

***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 Global Market, our securities are currently relatively thinly traded. Our current solvency concerns could serve to exacerbate the thin trading of our securities. 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 as a result of the solvency concerns. Accordingly, it may be difficult to sell shares of 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. Moreover, our stock price has generally been declining for the last 12 months. Although our common stock had a closing market price of \$1.33 as of December 12, 2008, our stock had a closing market value of less than \$1.00 at various points in October 2008, which is in violation of Nasdaq's standard continued listing requirements. Nasdaq has temporarily suspended the enforcement of rules requiring a minimum \$1.00 closing bid price, but this suspension is currently only in effect through January 16, 2009. Given the volatility of our stock price, there is no guarantee that we will be in compliance with Nasdaq's continued listing requirements when this suspension is lifted. If our stock is trading below \$1.00 when the temporary suspension is lifted, Nasdaq may commence delisting procedures against us. If we were to be delisted, the market liquidity of our common stock would likely be adversely affected and the market price of our common stock would likely decrease. Such a delisting could also adversely affect our ability to obtain financing for the continuation of our operations and could result in a loss of confidence by investors, suppliers and employees. In addition, our stockholders' ability to trade or obtain quotations on our shares could be severely limited because of lower trading volumes and transaction delays. These factors could contribute to lower prices and larger spreads in the bid and ask price for our common 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 will 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 our 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 would likely decline. If one or more of these analysts cease to cover our industry or us or fails to publish reports about our 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 its stock in a short period of time, the price of our stock may decline.

***We may be the target of securities class action litigation due to future stock price volatility.***

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.

***We do not intend to declare cash dividends on our common stock.***

We will not distribute cash to our stockholders until and unless we can develop sufficient funds from operations to meet our ongoing needs and implement our business plan. The time frame for that is inherently unpredictable, and you should not plan on it occurring 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 our 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 our 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. As a result, the issuance of the preferred stock could have a material adverse effect on the price of our common stock and could make it more difficult for a third party to acquire a majority of our outstanding common stock.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

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Our corporate headquarters is located in Pasadena, California. The Company leases the following facilities:

	Lab/Office Space	Monthly Rent	Lease Commencement	Lease Term
Arrowhead				
Pasadena(1)	7,388 sq ft	\$ 17,362	March 1, 2006	62 Months
New York(2)	130 sq ft	\$ 3,600	September 15, 2008	14 Months
Calando	4,354 sq ft	\$ 12,599	June 1, 2006	36 Months
Unidym				
Menlo Park, CA(3)	9,255 sq ft	\$ 14,345	February 1, 2007	36 Months
Sunnyvale, CA(3)	20,500 sq ft	\$ 25,625	October 1, 2008	60 Months
Springfield, MO	1,900 sq ft	\$ 2,533	December 1, 2007	24 Months
Houston, TX(4)	8,017 sq ft	\$ 13,362	February 1, 2007	Monthly
Pasadena, TX(4)	28,500 sq ft	\$ 18,200	September 1, 2008	120 Months

- (1) Arrowhead leases corporate office space in Pasadena, which it occupied beginning March 1, 2006. The lease agreement provides Arrowhead with two months free rent which was recorded as a deferred liability and is being amortized over the life of the lease.
- (2) In September 2005, Arrowhead opened an office in New York City and has one employee working out of that office. In September 2008, the lease was renewed for 12 months effective December 1, 2008.
- (3) Unidym is in the process of relocating its Menlo Park, CA operations to Sunnyvale and intends to sublease the Menlo Park facility for the remainder of the current lease.
- (4) Unidym is in the process of relocating portions of its Houston, TX manufacturing operations to Sunnyvale, CA. At the current time, it is Unidym's intent to sublease the Pasadena, TX location for the remainder of the lease term.

The Company has no plans to own any real estate and expects all facility leases will be operating leases.

Facility and equipment rent expense for the years ended September 30, 2008, 2007 and 2006 was \$1,075,524, \$870,289, and \$604,630, respectively. From inception to date, rent expense has totaled \$2,978,131.

**ITEM 3. LEGAL PROCEEDINGS**

The Company is not currently party to any material legal proceedings.

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

No matters were submitted to a vote of security holders during the fourth quarter of fiscal year ended September 30, 2008.

**Table of Contents****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 bid prices for a share of the Company's Common Stock during each period indicated. During the year ended September 30, 2008, the weekly trading volume ranged from 183,700 shares to 4,084,200 shares with an average weekly volume of 907,223 shares.

	Fiscal Year Ended September 30,			
	2008		2007	
	High	Low	High	Low
1st Quarter	5.01	3.36	5.30	4.13
2nd Quarter	3.55	1.90	4.63	3.60
3rd Quarter	3.07	2.13	7.60	4.48
4th Quarter	2.59	1.04	5.42	3.97

*Shares Outstanding*

At December 11, 2008, an aggregate of 42,934,517 shares of the Company's Common Stock were issued and outstanding, and were owned by \_\_\_\_\_ 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.

*Sales of Unregistered Securities*

The Company did not conduct any offerings of equity securities during the fourth quarter of 2008 that were not registered under the Securities Act of 1933.

*Repurchases of Equity Securities*

We did not repurchase any shares of our common stock during fiscal 2008 or fiscal 2007.

*Information Regarding Equity Compensation Plans*

The following table provides certain information as of September 30, 2008, with respect to all of the Company's equity compensation plans in effect on that date.

Plan Category	Equity Compensation Plan Information		
	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities

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				<b>reflected in column (a)</b>
Equity compensation plans approved by security holders(1)	6,007,632	\$	3.24	289,678
Equity compensation plans not approved by security holders(2)	2,000,000		3.92	
<b>Total</b>	<b>8,007,632</b>			<b>289,678</b>

(1) Includes the 2000 Stock Option Plan and the 2004 Equity Incentive Plan.

(2) Represents an inducement grant as part of the Company's CEO's compensation package.

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The table below presents selected consolidated financial data of Arrowhead and its Subsidiaries as of and for the years ended September 30, 2008, 2007, 2006, 2005, and 2004, derived from Arrowhead's audited consolidated financial statements included in this Annual Report on Form 10-K and prior years' reports filed on Form 10-K. Certain prior year amounts have been reclassified to conform to current year presentation or the retroactive application of FAS 123(R) and the sale of Aonex in 2008 and the discontinuance of Nanotechnica in 2005.

The selected consolidated financial data set forth below should be read in conjunction with our consolidated financial statements and related notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K.

**Arrowhead Research Corporation & Subsidiaries Selected Financial Data****Arrowhead Research Corporation****Selected Financial Data**

	Year Ended September 30,				
	2008	2007	2006	2005	2004
<b>Consolidated Statements of Operations Data:</b>					
<b>REVENUE</b>	\$ 1,303,201	\$ 1,208,022	\$ 461,280	\$ 580,683	\$ 196,306
<b>OPERATING EXPENSES</b>					
Salaries	13,720,561	10,011,266	5,474,018	2,524,234	381,923
Consulting	3,181,952	1,784,080	701,775	348,096	565,253
General and administrative	6,848,332	5,105,357	3,840,562	2,009,695	820,862
Research & development	12,144,529	20,983,824	8,300,838	2,898,345	643,155
Patents amortization	410,408	415,473	391,248	181,752	
<b>TOTAL OPERATING EXPENSES</b>	<b>36,305,782</b>	<b>38,300,000</b>	<b>18,708,441</b>	<b>7,962,122</b>	<b>2,411,193</b>
<b>OPERATING LOSS</b>	<b>(35,002,581)</b>	<b>(37,091,978)</b>	<b>(18,247,161)</b>	<b>(7,381,439)</b>	<b>(2,214,887)</b>
<b>OTHER INCOME (EXPENSE)</b>					
Loss on equity of investment	(114,729)				
Gain on sale of stock in subsidiary				2,292,800	
Unrealized (loss) in marketable securities			315,616	78,761	(12,113)
Interest	736,343	1,264,237	837,421	147,956	30,980
Other income		329		3,308	
<b>TOTAL OTHER INCOME (EXPENSES)</b>	<b>621,614</b>	<b>1,264,566</b>	<b>1,153,037</b>	<b>2,522,825</b>	<b>18,867</b>
<b>LOSS BEFORE MINORITY INTERESTS</b>	<b>(34,380,967)</b>	<b>(35,827,412)</b>	<b>(17,094,124)</b>	<b>(4,858,614)</b>	<b>(2,196,020)</b>
Minority interests	7,445,542	6,727,284	(126,532)	1,078,376	163,008
<b>LOSS FROM CONTINUING OPERATIONS</b>	<b>(26,935,425)</b>	<b>(29,100,128)</b>	<b>(17,220,656)</b>	<b>(3,780,238)</b>	<b>(2,033,012)</b>
Loss from discontinued operations - Nanotechnica, Inc.				(1,234,233)	(108,272)
Loss on disposal of Nanotechnica, Inc.				(73,797)	
Loss from discontinued operations - Aonex Technologies, Inc.	(459,949)	(830,990)	(1,776,553)	(1,766,650)	(354,858)
Gain on sale of Aonex Technologies	306,344				
Provision for income taxes					(800)

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NET LOSS \$ (27,089,030) \$ (29,931,118) \$ (18,997,209) \$ (6,854,918) \$ (2,496,942)

*Amounts per common share:*

Loss from continuing operations per share, basic and diluted	\$ (0.69)	\$ (0.81)	\$ (0.54)	\$ (0.20)	\$ (0.18)
Loss from discontinued operations per share, basic and diluted	(0.00)	(0.02)	(0.05)	(0.07)	(0.01)
Net loss per share, basic and diluted	(0.69)	(0.83)	(0.59)	(0.27)	(0.19)
Weighted-average shares, basic and diluted	39,191,298	35,867,091	31,953,806	18,725,263	11,002,094

**Consolidated Balance Sheet Data:**

Cash, cash equivalents and marketable securities	10,093,585	\$ 24,120,097	\$ 28,020,304	\$ 22,543,896	\$ 9,040,554
Working capital	8,176,818	22,409,053	25,855,557	21,789,931	8,807,377
Total assets	17,255,442	29,852,952	34,525,878	29,040,721	11,915,778
Current liabilities	2,384,299	2,896,375	2,920,234	1,024,064	689,698
Minority interest		152,609	934,438	1,889,190	1,777,699
Stockholders' equity	12,302,609	26,303,968	30,671,206	26,127,467	9,448,381

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

***Overview***

*Unless otherwise noted, (1) the term Arrowhead refers to Arrowhead Research Corporation, a Delaware corporation formerly known as InterActive Group, Inc., (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 the company Arrowhead (3) the term ARC refers to Arrowhead Research Corporation, a privately-held California corporation with which Arrowhead consummated a stock exchange transaction in January 2004, (4) the term Subsidiaries refers collectively to Calando Pharmaceuticals, Inc., Unidym, Inc., Agonn Systems, Inc. and Tego Biosciences Corporation and (5) the term Common Stock refers to Arrowhead Research's Common Stock and the term stockholder(s) refers to the holders of Common Stock or securities exercisable for Common Stock.*

Arrowhead is a nanotechnology holding company striving to bring new products to market via its subsidiaries and investments in the healthcare, electronics, and clean energy industries. Our mission is to create shareholder value by building Subsidiaries that may be monetized in three primary ways: (1) Subsidiaries may be sold to other companies with proceeds flowing back to Arrowhead; (2) Subsidiaries may execute an IPO, with proceeds flowing back to Arrowhead and/or providing Arrowhead with tradable stock; and (3) Subsidiaries may become mature operating units with earnings consolidated with Arrowhead. In the near-term, we are focused on maximizing the value of our most mature Subsidiaries, Calando Pharmaceuticals, Inc. and Unidym, Inc., through internal development, partnership and license arrangements, as well as pursuing new sources of cash investments. Our longer-term strategy for development and investment in existing Subsidiaries and minority investments will be determined by cash availability and the strength of technology and market opportunity. Arrowhead is continually identifying and developing business opportunities for new areas of investment which may be engaged as capital resources allow.

***Cash Resources***

As a development stage company, Arrowhead has historically financed its operations through the sale of securities of Arrowhead and its Subsidiaries. Development of products at our Subsidiaries, in particular Calando and Unidym, has required significant capital investment since the Company's inception in 2003 and will continue to require significant cash investment in fiscal 2009 for the Company to fund operations at historical levels. At September 30, 2008, Arrowhead had cash on hand of approximately \$10 million on a consolidated basis. The Company recognizes that if no additional cash resources are obtained, the Company must scale back its cash consumption to remain a going concern.

The Board has approved a strategy for the Company to conserve cash resources and seek sources of new capital. To execute on this strategy, the Board will seek to accomplish one or more of the following on favorable terms:

out-license of technology;

sale of a subsidiary;

sale of non-core assets;

funded joint development or partnership arrangements; and

sale of securities.

The Company is actively involved in discussions with third parties regarding many of these alternatives. Until such time as one or more of these goals is accomplished, the Company will continue to implement streamlining and cash conservation measures begun in fiscal 2008 and defer major investment in new initiatives. If no additional cash is obtained by mid second quarter 2009, the Company has a plan to make even deeper cuts in its development efforts at Calando and Unidym and reduce expenses at Arrowhead to insure that the Company has cash to fund operations in a limited manner through fiscal 2009 and into 2010.

***Majority-owned Subsidiaries***

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Arrowhead is highly active in the operation of its Subsidiaries, centralizing key management responsibilities at the Arrowhead level. Each Subsidiary is staffed with its own technical team that focuses on its specific technology and markets, while Arrowhead provides initial management and services including operational support, business development and financing. We believe this provides our Subsidiaries with significant competitive advantages. We previously retained management teams at Calando and Unidym to manage and grow their operations. Our board of directors determined that independent management teams at Calando and Unidym required significant cash and reduced the overall efficiency of the companies on a consolidated basis. During fiscal 2008 and in the first quarter of fiscal 2009, Calando and Unidym terminated senior management to conserve cash and consolidate financial and strategic operations at Arrowhead.

Arrowhead currently has two majority-owned Subsidiaries, two wholly owned subsidiaries (the Subsidiaries ), and has minority investments in two development stage nanotechnology companies. The Company s Subsidiaries seek to commercialize a variety of nanotech products and applications, including anti-cancer drugs, RNAi therapeutics, carbon-based electronics and fullerene anti-oxidants. The Company s minority investments are focused on developing advanced nanomaterials for spinal cord injury and wound healing and drug delivery technology. In fiscal 2008, the Company took significant steps to streamline operations at each of its majority-owned subsidiaries and to consolidate management at the Arrowhead level. The Company expects to continue this trend into fiscal 2009.

At September 30, 2008, the Company had two majority-owned, operating Subsidiaries, Calando Pharmaceuticals, Inc. ( Calando ) and Unidym, Inc. ( Unidym , formerly NanoPolaris, Inc.), and two wholly owned subsidiaries, Tego BioSciences Corporation ( Tego ) and Agonn Systems, Inc. ( Agonn ). In fiscal 2008, the Company acquired minority interest in two other nanotechnology companies, Nanotope, Inc. ( Nanotope ) and Leonardo Biosystems, Inc. ( Leonardo ) Arrowhead s business plan includes adding to its portfolio through selective acquisition and formation of new companies. As part of its model, the Company expects to create or acquire subsidiaries to commercialize promising technologies, close a subsidiary based upon lack of technical or business progress or sell a subsidiary if an attractive offer is received.



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### Calando

In the second quarter of fiscal 2008, the Company merged two majority owned Subsidiaries, Insert Therapeutics, Inc. and Calando to bring both drug delivery platforms into the same company. The merged company is operating under the name Calando Pharmaceuticals, Inc. At the same time, Calando shifted focus from preclinical and pipeline development to emphasize its clinical program. Consequently, Calando's operations were streamlined by reductions in executive and technical staff and the two facilities were consolidated. In connection with the reduction in Calando's executive management, Arrowhead took over the management of Calando. These actions reduced the consumption of cash for salaries and facilities, however, significant cash was consumed in fiscal 2008 in preparations to enter a second clinical trial, clinical trial expenses for Calando's Phase I study, and the development of a second RNAi therapeutic. Since the merger in April 2008, Arrowhead has made a series of cash advances totaling approximately \$5 million to fund Calando's operations. Calando's cash consumption fluctuates from quarter to quarter depending on the progress of its projects, but in fiscal 2008, it has ranged between \$2.2 million and \$2.6 million per quarter. If Calando is unsuccessful in attracting additional capital and Arrowhead does not have sufficient cash resources to support Calando's operations, some or all of Calando's development projects would have to be scaled back, interrupted, or abandoned in order to manage cash so that Calando limited operations through fiscal 2009 and into 2010.

Subsequent to September 30, 2008, Calando raised \$2.7 million of additional funds through the sale of senior unsecured convertible promissory notes ( New Notes ) (of which \$1.1 million has been received), in which financing, Arrowhead participated by buying \$200,000 of the New Notes and agreeing to subordinate principal and interest on Arrowhead's \$5.3 million of demand notes to the New Notes sold. The New Notes have a 2 year maturity and bear 10% interest compounded annually. Unpaid principal of the Note and accrued but unpaid interest thereon is convertible into common stock of Calando at a conversion price of \$0.576647 per share, subject to adjustment, at any time in the sole discretion of the holder. In the event of a defined sale event holders of New Notes have other exchange and conversion options.

Calando Pharmaceuticals is Arrowhead's most mature biopharmaceutical subsidiary. Based on technology developed at the California Institute of Technology, Calando's proprietary linear cyclodextrin nanoparticle technology is designed to deliver small molecule drugs using Calando's Cyclosert™ system and RNAi therapeutics using the RONDEL™ system. Using these platform systems, Calando has developed two anti-cancer drug candidates that are currently undergoing human clinical trials. The Company believes that Calando is an attractive near term partnership candidate or acquisition target for several pharmaceutical and biotech companies that are active in the development of RNAi therapeutics. Systemic delivery has posed a major hurdle to the clinical development of siRNA therapeutics. Calando is in ongoing discussions with multiple potential partners and acquirers.

Calando's RONDEL-enabled siRNA-based therapeutic, CALAA-01, is currently undergoing a phase I clinical trial in patients with solid tumors at the UCLA Jonsson Cancer Center in Los Angeles, California, and at South Texas Accelerated Research Therapeutics (START) in San Antonio, Texas. CALAA-01 targets the expression of the M2 subunit of ribonucleotide reductase, a clinically validated cancer target. To our knowledge, Calando is the first and only company with a clinical stage systemic delivery system enabled siRNA therapeutic. Further, we believe CALAA-01 is also the only clinical stage siRNA therapeutic candidate for the treatment of cancer. Although this study has only recently begun, it has progressed without complications. Additionally, Calando is performing preclinical studies on CALAA-02, a second RONDEL-enabled anti-cancer siRNA therapeutic candidate targeting expression of the hypoxia inducible factor-2 alpha gene.

Calando's other nano-engineered polymer delivery system, Cyclosert, is designed to deliver small molecule drugs and peptides. IT-101, Calando's first clinical small molecule candidate, is a combination of Cyclosert and Camptothecin, a potent anti-cancer therapeutic. A Phase I trial for IT-101 was completed in October 2008. All Phase I trial endpoints were successfully achieved. The drug was found to be well tolerated in both the Phase Ia and Ib studies of the trial. In addition, a high proportion of patients displayed stable disease following treatment. Based on these encouraging Phase I results, Calando has opened a Phase II trial for ovarian cancer.

We believe there is opportunity to derive additional value from the further development of Cyclosert and RONDEL systems, as they have been demonstrated to enhance and enable the delivery of multiple pharmaceutical entities, including peptides and small molecules as well as other RNA and DNA-based oligonucleotides. CALAA-02 is being developed to demonstrate the fast track to the clinic that can be provided by the RONDEL system. Also, Calando is applying its library of Cyclosert linkers to develop new conjugate oncology therapeutics with the goal of improving the efficacy and side effect profile of generic and in-licensed compounds. Ultimately, the Company believes Calando provides a platform opportunity that could enable the creation of multiple new drug candidates. Continuation of Calando clinical and pipeline candidates could be limited by the capital resources available. In order to fund continued development, subsequent to September 30, 2008, Calando has signed agreements to issue \$2.7 million in New notes of which \$1.1 million has been received and is seeking an additional \$2.3 million. If Calando is unable to secure additional funding, and Arrowhead has insufficient capital to loan or invest in Calando, Calando's development efforts could be slowed or interrupted. Arrowhead owns 64% of the outstanding stock of Calando. If Calando raises substantial outside capital to fund operations, Arrowhead's ownership interest could be diluted.

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Calando's efforts on CALAA-01, IT-101 and its other pipeline candidates are preliminary, and there is no assurance that they will be successful. There are numerous technical, regulatory and marketing challenges that must be overcome to successfully commercialize Calando's products, including, but not limited to the following:

Advancing Calando's pipeline candidates requires extensive preclinical testing and approval by the FDA is required before clinical testing can commence.

Advancing Calando's therapeutic candidates through preclinical and clinical testing is expensive and takes a long time.

Complications may arise that would cause the clinical testing to be interrupted or stopped. FDA approval is required before Calando's products could be sold.

Even if FDA approval is eventually obtained, there is no assurance that it will be accepted by the medical community. It is not possible at this time to accurately determine the final cost of Calando's development projects, the completion dates, or when or if revenue will commence.

### Unidym

Unidym raised a total of \$14 million of equity financing in fiscal 2008. In fiscal 2008, Unidym consumed large amounts of cash to scale up the manufacture of carbon nanotubes, scale up for the production and sale its first carbon nanotube based film product, acquire another nanotech company, expand its business development activities, and prepare for an initial public offering. In the first and second quarters of fiscal 2008, Unidym expanded its executive, technical and administrative staff for these activities. Unidym's cash burn ramped from \$2 million in the second quarter, \$3.6 million in the third quarter and \$4.2 million in the fourth quarter. In the fourth quarter, it was clear that Unidym would be unable to meet its fund raising goals to support its 2009 cash needs. Moreover, technical development took longer than expected. Additionally, it became evident that dramatic change in the financial market would not allow an initial public offering. Starting in October 2008, several general and administrative positions were eliminated. Approximately, half of its team in its Houston, TX facility was put on unpaid leave to conserve cash. Further cuts to personnel and consolidation of facilities are planned to bring Unidym's cash burn to 60% of its high water mark in fourth quarter 2008. However, Unidym will still need to obtain additional cash to fund its operations and obligations through fiscal 2009.

Subsequent to September 30, 2008, Unidym raised \$2 million from the sale of Series C-1 Preferred Stock to TEL Ventures. The sale of these securities was associated with Unidym's entry into a Security Agreement granting TEL a security interest in Unidym's physical and intellectual property (the Collateral; which, however, excludes Unidym's rights under the Rice license and shares of Ensycse Biosciences, Inc.). The Subscription Agreement provided TEL with two put options. TEL may exercise the first put option if Unidym fails to enter into a Joint Development Agreement with TEL by June 30, 2009. In that case, Unidym must buy back TEL's Unidym shares for \$2 million before March 2010. TEL may exercise the second option if Unidym fails to meet certain cash requirements by June 30, 2009. Those requirements would be met if Unidym raises \$7 million through any combination of a sale of its equity; the sale or license of some or all of its assets and businesses including positions in Ensycse Biosciences, Nexeon MedSystems or Nanoconduction; or sales of products. Only if TEL exercises this put option between June 30 and July 31, 2009, shall Unidym be obligated to repurchase the Series C-1 Preferred Stock for \$2.4 million within ten days notification of exercise. In the event of a default under the Security Agreement, e.g., inability to pay either of the put options, bankruptcy, admission of inability to pay its bills; TEL can take possession of the Collateral and keep net proceeds of any sale thereof.

A material portion of Unidym's intellectual property portfolio is exclusively licensed from Rice University. If the sum of Unidym's debts, liabilities and other obligations is greater than all of Unidym's assets at fair valuation or if Unidym is generally not paying its debts, liabilities and other obligations as they come due; the Rice license would terminate.

Unidym is the Company's most mature nanomaterials company and provides an example of a company-building strategy that Arrowhead plans to replicate in other areas of nanotechnology. Through the acquisition of a foundational intellectual property portfolio in the manufacture and applications of carbon nanotubes (CNTs), Unidym has developed a strong technology base in CNT technology that we believe can serve as a platform for innovation and new products. Unidym has already developed world-leading high performance carbon nanotube materials manufactured by scalable processes. Unidym's product development efforts are focused on the electronics industry, where there is continuing demand for higher performance materials. Unidym's product development has been focused on thin, transparent film of carbon nanotubes on a flexible substrate. Unidym is also working with leading LCD companies, including a joint development agreement with Samsung Electronics, to incorporate CNT films into their display devices. Through its various collaborations, Unidym has also fabricated prototype LCD and electrophoretic displays incorporating CNT-based films.



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The capital expenditures associated with CNT synthesis are kept low by both the scalability of Unidym's CNT synthesis process and the fact that only trace amounts of CNTs are required per unit area of film. Additionally, Unidym can leverage the substantial excess capacity left in the coating industry by the decrease in demand for photographic film. For its initial product offering to touch panel makers, Unidym is currently evaluating the most favorable business model to pursue. In one model, Unidym would synthesize CNTs, formulate those CNTs into a coating ink, and outsource production of the films to a toll coater to produce the film. Unidym would pay for production of the films on a time and materials basis, and Unidym would directly market and sell the films to touch panel makers. Under a second model that is less capital intensive, Unidym would synthesize CNTs and CNT inks, and then ship the inks to company that would manufacture and sell films to touch panel makers.

Unidym's facilities in Houston, Texas have historically provided bulk CNT materials to customers primarily for research or early commercial prototyping processes. This activity has provided modest revenues for Unidym. The lease on the Houston facility has been terminated and Unidym must vacate the premises in the near future. Unidym has decided not to occupy its new facility in Houston and is currently evaluating whether to continue to sell bulk CNT materials. The facility in Houston also provides materials for Unidym's CNT film product. Unidym is currently exploring more cost effective alternatives to produce CNTs for its film product than operating its Houston facility. Alternatives include moving its production capabilities to its Sunnyvale facility or outsourcing CNT production to a third party. If Unidym decides to move its production capabilities for CNTs Sunnyvale, it will incur significant costs for the retrofit and the time required could result in a delay in bringing Unidym's products to market and an interruption or cessation of Unidym's revenues.

Development, production and sale of Unidym's products have required and is expected to continue to require significant investment and to take a long time. There are a variety of technical, cost, and marketing barriers that must be overcome. It is not possible at this time to predict the final cost of developing Unidym's transparent conductive film or other CNT products, the final cost of scaling up the production process, when or if Unidym will generate significant licensing revenue, or when or if Unidym will become profitable.

In July 2008, Unidym acquired Nanoconduction, Inc., a Sunnyvale, CA company developing nano-based electronic cooling technology ( Nanoconduction ). The merger provides Unidym with access to Nanoconduction's patent portfolio, which will supplement Unidym's existing patent portfolio and provides Unidym with additional opportunities to out-license and leverage its technology. In addition, through the merger, Unidym will gain access to research facilities and equipment that will be used in Unidym's ongoing research and development activities.

Unidym accomplished the acquisition of Nanoconduction through an equity exchange, as follows. Arrowhead invested \$250,000 in Unidym through a cashless investment by issuing 114,115 shares of unregistered Common Stock to the owners of Nanoconduction. In exchange for this investment, the Company received 138,889 additional shares of Series C Preferred Stock of Unidym. As additional consideration, Unidym agreed to assume and discharge Nanoconduction's assets and liabilities. Assets included equipment and leasehold improvements with an estimated net book value of approximately \$2.9 million including intellectual property related to the use of carbon nanotubes for thermal management. Liabilities included approximately \$1.0 million of accounts payable and accrued liabilities and approximately \$1.7 million in capital equipment loans. The equipment loans are guaranteed by Unidym and secured by a lien on Nanoconduction assets. Unidym entered into a new five-year lease for the facilities currently occupied by Nanoconduction in Sunnyvale, California, with the intention of moving Unidym's existing Menlo Park operations to the Nanoconduction facility.

In March 2008, Unidym sub-licensed certain of its intellectual property to Ensysce BioSciences Inc. ( Ensysce ) whose focus is research into the medical therapeutic applications of carbon nanotubes. From March 2008 to November 2008, Ensysce was both funded and effectively controlled by a related party to Unidym who also serves as a director of Unidym. In November 2008, Unidym sold its 50 percent interest in Ensysce to the controlling shareholder for \$700,000, and will recognize a gain on the sale during the first quarter of fiscal 2009.

### Tego

Tego's primary asset is an intellectual property portfolio that includes key patents for the modification of fullerenes. Tego does not control the intellectual property relating to making fullerenes, however we believe that it does control key patents that are critical in making fullerenes into useable products. We believe Tego is in a position to monetize its proprietary compounds and enabling patents through a licensing and partnership model. Currently, Tego has no employees or facilities and its technical and business development is handled at the Arrowhead level. Tego is in discussions with other companies regarding potential partnerships and licenses which could enable Arrowhead to capture value via near-term revenue, as well as long-term royalties. Tego's development and licensing activities are preliminary, and there is no assurance that they will be successful. It is not possible at this time to accurately determine the final cost of developing or licensing Tego's technology, the completion date, or when or if revenue will commence.

### Agonn

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Agonn Systems Corporation is Arrowhead's newest Subsidiary, formed in 2008 to develop and commercialize nanotechnology-based energy storage devices for electric vehicles and other large format applications. Agonn is pursuing a strategy to acquire energy storage technologies based on nanoscale engineering from research institutions. Agonn has outsourced the development of prototype ultracapacitors based on carbon nanomaterials and other advanced materials. We believe the markets for energy storage products are substantial, ranging from consumer electronics to vehicles to heavy industry and that emerging clean technology platforms offer significant market opportunities for new energy storage devices, in part because traditional batteries do not meet many of the key requirements for energy density, lifetime and efficiency.

Agonn has no facilities or employees and is managed entirely by Arrowhead. At September 30, 2008, Agonn was a wholly-owned subsidiary of the Company. The Company expects that this ownership interest may be diluted in the future with the issuance of equity to strategic partners. Agonn's research and development activities are preliminary, and there is no assurance that they will be successful. It is not possible at this time to accurately determine the final cost of developing Agonn's technology, the completion date, or when or if revenue will commence.

### **Minority Investments**

#### *Nanotope*

Nanotope is a company in the field of regenerative medicine developing a suite of products customized to regenerate specific tissues; including neuronal, vascular, bone, myocardial, and cartilage. Its two lead candidates are focused on spinal cord regeneration and treatment of peripheral artery disease.

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The Company acquired its initial stake in Nanotope from a Nanotope shareholder in April 2008 and increased its position through a direct investment of \$2M in two tranches of \$1 million each in July and September 2008. At September 20, 2008, the Company owned 22% of Nanotope's outstanding securities. The Company may increase its stake in Nanotope if the opportunity arises, the Company has the capital resources and Nanotope's technology development continues to move forward. The Company's investment in Nanotope is accounted for using the equity method of accounting.

### **Related Party Interests**

Nanotope was co-founded by the Company's President and Chief Executive Officer, Dr. Christopher Anzalone, through the Benet Group, a private investment entity solely owned and managed by Dr. Anzalone. Through the Benet Group Dr. Anzalone owns 1,395,900 shares of Nanotope common stock, or approximately 14.2% (after giving effect to the sale of stock to Arrowhead in its investments in Nanotope) of Nanotope's outstanding voting securities. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Nanotope directly or through the Benet Group. The Benet Group has the right to appoint a representative to the board of directors of Nanotope. Dr. Anzalone currently serves on the Nanotope board in a seat reserved for Nanotope's CEO and another individual holds the seat designated by the Benet Group. Dr. Anzalone has served as President and Chief Executive Officer of Nanotope since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Nanotope since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Nanotope before he joined the Company.

### ***Leonardo Biosystems, Inc.***

Leonardo is a drug delivery company that employs a novel strategy aimed at dramatically increasing targeting efficiency. Leonardo has licensing agreements and contract research agreements with UT Houston for production of preclinical amounts of nanoparticles. Animal testing suggests that Leonardo's platform enables significantly increased targeting. The Company currently owns 6% of Leonardo. The Company is interested in increasing its stake in Leonardo if the opportunity arises, the Company has the capital resources and Leonardo's technology development continues to move forward. The Company's investment in Leonardo is accounted for using the cost method of accounting.

### **Related Party Interests**

Like Nanotope, Leonardo was co-founded by the Company's President and Chief Executive Officer, Dr. Christopher Anzalone, through the Benet Group, a private investment entity solely owned and managed by Dr. Anzalone. Through the Benet Group Dr. Anzalone owns 918,750 shares of Leonardo common stock, or approximately 17% of the outstanding stock of Leonardo. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Leonardo directly or through the Benet Group. The Benet Group has the right to appoint a representative to the board of directors of Leonardo. Dr. Anzalone currently serves on the Leonardo board in a seat reserved for Leonardo's CEO and another individual holds the seat designated by the Benet Group. Dr. Anzalone has served as President and Chief Executive Officer of Leonardo since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Leonardo since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Leonardo before he joined the Company.

### ***Aonex Discontinued Operation***

In 2007, Arrowhead determined that in order to monetize its investment in majority owned subsidiary Aonex Technologies, Inc., it should seek to partner its technology with another company with greater financial resources and market reach. In May 2008, Arrowhead sold its stake in Aonex to New Hampshire based Amberwave Systems, Inc. for upfront and milestone payments of up to \$7.5 million plus a royalty on solar products or licenses. Amberwave took over Aonex's Pasadena, California operations and is continuing to develop Aonex's technology. The losses incurred by Aonex are segregated in the Consolidated Statement of Operations as Loss from Discontinued Operation Aonex.

### ***Academic Partnerships***

In prior years, Arrowhead devoted significant capital resources to sponsored research. As the Subsidiaries have matured, the Company has decreased its reliance on sponsored research for technology development and sponsored research expense has decreased. As of September 30, 2008, Arrowhead had one active sponsored research agreement at Duke University through Unidym. Depending on capital resources, Arrowhead is likely to continue to invest in nanoscience research and development through sponsored research agreements at universities.

### **Factors Affecting Further R&D Expenses**

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The Company expects that research and development expenses will continue to increase in the foreseeable future as it adds personnel, expands its pre-clinical research, begins clinical trial activities, and increases its regulatory compliance capabilities. The amount of these increases is difficult to predict due to the uncertainty inherent in the timing and extent of progress in the Company's research programs. As the Company's research efforts mature, it will continue to review the direction of its research based on an assessment of the value of possible commercial applications emerging from these efforts.

In addition to these general factors, specific factors that will determine the eventual cost to complete the current projects at Calando include the following:

the number, size and duration of clinical trials required to gain FDA approval;

the costs of producing supplies of the drug candidates needed for clinical trials and regulatory submissions;

the efficacy and safety profile of the drug candidate; and

the costs and timing of, and the ability to secure, regulatory approvals.

It is possible that the completion of studies could be delayed for a variety of reasons, including difficulties in enrolling patients, delays in manufacturing, incomplete or inconsistent data from the pre-clinical or clinical trials, and difficulties evaluating the trial results. Any delay in completion of a trial would increase the cost of that trial, which would harm the Company's results of operations. Due to these uncertainties, the Company cannot reasonably estimate the size, nature nor timing of the costs to complete, or the amount or timing of the net cash inflows from Insert or Calando's current activities. Until the Company obtains further relevant pre-clinical and clinical data, it will not be able to estimate its future expenses related to the Subsidiaries' programs or when, if ever, and to what extent, the Company will receive cash inflows from resulting products.

### ***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

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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 exists that an arrangement exists, title had passed and delivery has occurred, a price was fixed and determinable, and collection was reasonably assured.

We may generate revenue from product sales, technology licenses, collaborative research and development arrangements, and research grants. 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 up-front license fees and 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 substantive milestones and future product royalties is 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.

### *Research and Development Expenses*

Research and development expenses include salaries and benefits, trial (including pre-clinical, clinical and other) and production costs, purchased in-process research expenses, contract and other outside service fees, and facilities and overhead costs related to our research and development efforts. Research and development expenses also consist of costs incurred for proprietary and collaborative research and development. Research and development costs are expensed as incurred.

### *Impairment of Long-lived Assets*

We review our 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 an impairment is indicated, the asset is written down to its estimated fair value based on quoted fair market values.

### *Valuation of Goodwill*

In accordance with *Statement of Financial Accounting Standards*, or SFAS, No. 142, *Goodwill and Other Intangible Assets*, we review goodwill (if any) for impairment annually and whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Goodwill is tested for impairment by comparing the fair value of the single reporting unit to its carrying value. If the implied fair value of goodwill is less than its carrying value, an impairment charge would be recorded.

### *Intellectual Property*

Intellectual property consists of patents and patent applications internally developed, licensed from universities or other third parties or obtained through acquisition. Patents and patent applications are reviewed for impairment whenever events or circumstances indicate that the carrying amount may not be recoverable, and any impairment found is written off. Licensed or internally developed patents are written off over the life of the patent unless impairment occurs. Purchased patents are written off over three years, unless an impairment occurs sooner.

## **Results of Operations**

The Company had a consolidated loss of approximately \$27.1 million for the year ended September 30, 2008, compared to a consolidated loss of \$29.9 million and \$19.0 million for the years ended September 30, 2007 and 2006, respectively.

The decrease in the fiscal 2008 consolidated loss over fiscal 2007 and fiscal 2006 is the result of a number of factors. First, there was a non-recurring expense of \$9,597,000 in 2007 for purchased in-process research and development related to Unidym's merger with CNI. Secondly, there was a reduction of approximately \$3 million in Calando's fiscal 2008 outside lab and contract services expense. Calando incurred major expenses during fiscal 2007 related to preclinical research, preparation for the filing of its Investigational New Drug application (IND) with the U.S. Food and Drug Administration, ( FDA ) for CALAA-01, obtaining sufficient drug inventories to be able to enter phase I clinical



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trials with CALAA-01, and payment for preparation required to enter the trials. With the initiation of the phase I trial for CALAA-01, the need in 2008 to incur outside labs and contract service expenses was reduced. Salary expense continued to increase in fiscal 2008 as the Company bolstered its management team at Arrowhead and Unidym. Unidym's rapid growth started in July of 2006 and accelerated with the merger with CNI in April 2007.

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In 2007 and 2006, staff increased at Calando to accommodate the increase in development efforts of new products and of the IND to be filed by Calando. Also in fiscal 2007, legal expenses increased as the Company completed the merger with CNI, a private placement for Calando and a private placement for Arrowhead.

In fiscal 2009, significant expense is expected to be incurred in the manufacture of the components for CALAA-02, preparation for an IND for CALAA-02 and the continuation of Calando's clinical trials. Continued clinical and preclinical development of Calando's drug candidates will depend on the cash resources available to Calando. Significant expense is expected to be incurred in the further development of Unidym's products. It is expected that an alternative source for carbon nanotubes will be identified or manufacture of carbon nanotubes will be consolidated with Unidym's product development facility in California. This is expected to result in reduced cash consumption in Texas which would be partially offset by costs necessary to relocate the production capability in California. The goal is to reduce development costs at Unidym substantially and the pace of development will depend on the cash resources available to Unidym. It is expected that the trend to consolidate management of the Subsidiaries at Arrowhead will continue with the goal to reduce cash outlay throughout the Company.

**Revenues**

The Company generated revenues of \$1,303,000, \$1,208,000 and \$595,000 for the three years ended September 30, 2008, 2007 and 2006, respectively. The revenue for the year ended September 30, 2008 consists of \$570,000 from grants to fund research for the development of carbon nanotube applications, \$85,000 from license fees from Unidym technology, and \$648,000 from the sale and delivery of carbon nanotubes to third parties. The revenue for fiscal 2007 consists of \$874,000 from grants to fund research for the development of carbon nanotube applications, \$326,000 from the sale and delivery of carbon nanotubes to third parties and \$8,000 for in residual funded research. The \$461,000 of revenue in 2006 resulted from a commercial license fees when Calando granted an exclusive worldwide license to Benitec Ltd. (ASX:BLT) for the combination of Calando's polymeric RNAi delivery technology with Benitec's RNAi-based therapeutic for the hepatitis C virus. The license was terminated by mutual agreement in July 2006. Revenues in 2009 cannot be estimated as Unidym is re-evaluating its strategy with regard to the sale of bulk carbon nanotubes and it is not clear when Unidym may have revenue from film sales.

**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 three years ended September 30, 2008, 2007 and 2006, are shown in the tables below. Prior period amounts have been reclassified to conform to the current period presentation. The amounts for each period have been adjusted to include the adoption of SFAS 123R and the sale of Aonex and its inclusion in discontinued operations.

**Salary & Wage Expenses**

Arrowhead employs management, administrative and technical staff at the Arrowhead corporate offices and the Subsidiaries. Salary and wage expense consists of salary, benefits, and non-cash charges related to equity based compensation in the form of stock options. Salary and benefits are allocated to two major categories: general and administrative compensation related expense and research and development compensation related expense depending on the primary activities of each employee. The following table details salary and related expenses for fiscal 2008, fiscal 2007 and fiscal 2006.

(in thousands)

	Year Ended September 30, 2008	% of expense category	Year Ended September 30, 2007	% of expense category	Year Ended September 30, 2006	% of expense category
G&A compensation-related	\$ 6,675	49%	\$ 4,376	44%	\$ 2,125	39%
Stock-based compensation	3,187	23%	2,176	22%	1,369	25%
R&D compensation-related	3,858	28%	3,459	34%	1,948	36%
Total	\$ 13,720	100				