ARRAY BIOPHARMA INC
Form 10-K
August 15, 2008
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U.S. SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended June 30, 2008

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-31979

Array BioPharma Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**84-1460811**
(State of Incorporation)	(I.R.S. Employer Identification No.)

3200 Walnut Street

Boulder, Colorado 80301

(Address of Principal Executive Offices)

(303) 381-6600

(Registrant s Telephone Number, Including Area Code)

Common Stock, Par Value $.001 per Share

(Securities Registered Pursuant to Section 12(b) of the Act)

The NASDAQ Stock Market LLC (NASDAQ Global Market)

(Name of Exchange on Which Registered)

None

(Securities Registered Pursuant to Section 12(g) of the Act)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act.

Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days.

Yes x No o

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. o

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 o Accelerated Filer x Non-Accelerated Filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes o No x

The aggregate market value of voting stock held by non-affiliates of the registrant as of December 31, 2007 (based upon the closing sale price of such shares as of the last trading day of the year, December 31, 2007, on the NASDAQ Global Market) was $397,452,106. Shares of the Registrant s common stock held by each executive officer and director and by each entity that owns 5% or more of the Registrant s outstanding common stock have been excluded in that such persons or entities may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

Number of shares outstanding of the registrant s class of common stock as of August 7, 2008: 47,557,131.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement to be filed with the Securities and Exchange Commission on Form 14A for the 2008 Annual Meeting of Stockholders are incorporated by reference in Part III of this Annual Report on 10-K to the extent stated therein.

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PART I

Array BioPharma Inc., the Array BioPharma Inc. logo and all other Array names are trademarks of Array BioPharma Inc. in the United States of America and in other selected countries. All other brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to Array, we, us, and our refer to Array BioPharma Inc.

FORWARD-LOOKING STATEMENTS

This Annual Report filed on Form 10-K and other documents we file with the Securities and Exchange Commission contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve significant risks and uncertainties. In addition, we may make forward-looking statements in our press releases or in other oral or written communications with the public. These forward-looking statements include, but are not limited to, statements concerning our projected timelines for the initiation and completion of preclinical and clinical trials; the potential for the results of ongoing preclinical or clinical trials to support regulatory approval or the marketing success of drug candidates; our plans with respect to the timing and scope of the expansion of our clinical and commercialization capabilities; other statements regarding our future product development and regulatory strategies, including with respect to specific indications; the ability of third-party contract manufacturing parties to support our drug development activities; any statements regarding our future financial performance, results of operations or sufficiency of capital resources to fund our operating requirements; and any other statements which are other than statements of historical fact.

Although we believe the assumptions upon which our forward-looking statements are based currently to be reasonable, our actual results could differ materially from those anticipated in these forward-looking statements as a result of many factors. These factors include, but are not limited to, our ability to continue to fund and successfully progress internal research and development efforts and to create effective, commercially viable drugs; our ability to effectively and timely conduct clinical trials in light of increasing costs and difficulties in locating appropriate trial sites and in enrolling patients who meet the criteria for certain clinical trials; our ability to achieve and maintain profitability; the extent to which the pharmaceutical and biotechnology industries are willing to in-license drug candidates for their product pipelines and to collaborate with and fund third parties on their drug discovery activities; our ability to out-license our proprietary candidates on favorable terms; risks associated with our dependence on our collaborators for the clinical development and commercialization of our out-licensed drug candidates; the ability of our collaborators and of Array to meet objectives tied to milestones and royalties; our ability to attract and retain experienced scientists, and management; and the risk factors set forth below under the caption Item 1A. Risk Factors. We are providing this information as of the date of this report. We undertake no duty to update any forward-looking statements to reflect the occurrence of events or circumstances after the date of such statements or of anticipated or unanticipated events that alter any assumptions underlying such statements.

ITEM 1 - BUSINESS

Our Business

We are a biopharmaceutical company focused on the discovery, development and commercialization of targeted small molecule drugs aimed at large market opportunities. Our proprietary drug development pipeline includes clinical candidates that are designed to treat patients afflicted with cancer, inflammatory diseases and pain. In addition, leading pharmaceutical and biotechnology companies collaborate with us to discover

and develop drug candidates across a broad range of therapeutic areas. We currently have six wholly-owned programs in our development pipeline:

- ARRY-797, a p38 inhibitor and pan-cytokine modulator for inflammation and for pain;
- ARRY-162, a MEK inhibitor for inflammation;
- ARRY-614, a p38/Tie 2 dual inhibitor for cancer and/or inflammation;
- ARRY-543, an ErbB family (EFGR / ErbB-2) inhibitor for cancer;
- ARRY-520, a KSP inhibitor for cancer; and
- ARRY-380, an ErbB-2 inhibitor for cancer.

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We also have a portfolio of drug discovery programs that we believe will generate one to three Investigational New Drug, or IND, applications each year. Our drug discovery efforts have also generated additional early-stage drug candidates that we may choose to out-license through research partnerships prior to filing an IND application.

Our Strategy

We are building a fully integrated, commercial-stage biopharmaceutical company that invents, develops and markets safe and effective small molecule drugs to treat patients afflicted with cancer, inflammatory diseases or pain. We intend to accomplish this through the following strategies:

- Inventing targeted small molecule drugs that are either first-in-class or second generation drugs that demonstrate a competitive advantage over drugs on the market or in clinical development;

- Partnering select drugs after establishing proof-of-concept for co-development and commercialization, while retaining the right to commercialize and/or co-promote in the U.S.;

- Partnering select early-stage programs for continued research and co-development in exchange for research funding, plus significant milestone payments and royalties;

- Expanding our clinical development organization to provide timely, robust proof of concept, and, in the longer term, to conduct later-stage development and seek marketing approval for important new drugs across multiple therapeutic areas; and

- Building commercial capabilities to position our drugs to maximize their overall value. As our first drug nears approval, we plan to build a U.S.-based, therapeutically-focused sales force to commercialize or co-promote our drugs.

Business History

We have built our proprietary pipeline of drug development and discovery programs on an investment of approximately $240 million from our inception through June 30, 2008. Over the past three years, research and development expenses for proprietary drug discovery have significantly increased year over year to support, in particular, our clinical development efforts and were $90.3 million for fiscal 2008, as compared to $57.5 million for fiscal 2007 and $33.4 million for fiscal 2006.

Additionally, we have received a total of $322 million in research funding and in up-front and milestone payments from our collaboration partners through June 30, 2008. Under our existing collaboration agreements, we have the potential to earn $1.4 billion in additional milestone payments if all the discovery and revenue objectives detailed in these agreements are achieved, as well as to earn royalties on any resulting product sales from 18 drug development programs.

Our three largest existing collaborators include:

- AstraZeneca, PLC, which licensed three of our MEK inhibitors for cancer, including AZD6244 (ARRY-886), which is currently in multiple Phase 2 clinical trials;

- Genentech, Inc., which entered into a worldwide strategic collaboration agreement with us to develop two of our cancer programs which has been expanded to include two additional cancer programs all four of which are in preclinical development; and

- Celgene Corporation, which entered into a worldwide strategic collaboration agreement with us focused on the discovery, development and commercialization of novel therapeutics in cancer and inflammation.

Through collaborations, we have also invented drug candidates that are currently in clinical development, including InterMune, Inc. s hepatitis C virus NS3/4 protease inhibitor, ITMN-191, and Eli Lilly and Company s (formerly ICOS Corporation) CHK-1 inhibitor, IC83. Our out-license and collaboration agreements with these and our other partners typically provide for up-front payments, research funding, success-based milestone payments and/or royalties on product sales.

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The following chart shows our six most advanced wholly-owned compounds, their stage in the drug development process and our expected future development plans.

Drug Candidates		Current Development Status	Expected Development Plan
Inflammation & Pain			
ARRY-797	P38	Phase 2 dental pain trial and Phase 1b 28-day rheumatoid arthritis, or RA, trial	Initiate Phase 2 ankylosing spondylitis trial during the second half of calendar 2008
ARRY-162	MEK	Phase 2 worldwide, 12-week RA trial	Receive top-line results during the second half of calendar 2009
ARRY-614	P38/Tie2	Phase 1 trial with healthy volunteers	Initiate first-in-patient Phase 1b trial in cancer and/or inflammation during the first half of calendar 2009
Cancer			
ARRY-543	ErbB-2/EGFR	Phase 1 expansion and Phase 1b/2 trials in metastatic breast cancer	Initiate combination studies with Xeloda® (capecitabine) and Taxotere® (docetaxel) in the second half of calendar 2008
ARRY-520	KSP	Phase 1 expansion trial and Phase 2 acute myelogenous leukemia, or AML, trials	Initiate Phase 2 multiple myeloma trial in the first half of calendar 2009
ARRY-380	ErbB-2	Phase 1 trial with cancer patients	Initiate Phase 1b combination trial during the first half of 2009
ARRY-614	P38/Tie2	Phase 1 trial with healthy volunteers	Initiate first-in-patient Phase 1b trial in cancer and/or inflammation during the first half of calendar 2009

Proprietary Development Programs

ARRY-797 - Pan-cytokine / p38 Program

p38 is a critical mediator of pain and inflammation, which acts by modulating the production of the pro-inflammatory cytokines TNF, IL-6 and IL-1 as well as the pain mediator PGE2. ARRY-797 is a novel, selective, potent inhibitor of p38 with unique physical properties. It is highly selective with nanomolar potency, high water solubility and low potential to cross the blood brain barrier. In a Phase 1 clinical trial in healthy volunteers, ARRY-797 demonstrated dose-dependent marked suppression of all three of these cytokines, as measured in *ex vivo* LPS-stimulated whole blood samples. We believe that inhibition of p38 will modulate cytokine production in various inflammatory disorders and, as such, ARRY-797 will be evaluated for a variety of painful, inflammatory indications.

Our clinical development activities for ARRY-797 consisted of the following during fiscal 2008:

- Conducted a Phase 2 trial in acute inflammatory pain using a dental pain model. ARRY-797 achieved its primary and secondary endpoints for analgesic effect, was well tolerated, and prevented the rise in C-reactive protein that follows oral surgery.

- Initiated a second Phase 2 acute inflammatory pain trial in 250 patients, in which we compared three doses of ARRY-797 (200, 400 and 600 mg) with both placebo and with an active comparator, Celebrex® (celecoxib) (400 mg).

During fiscal 2009, we plan to initiate the following studies:

- A 28-day Phase 1 study in 30 rheumatoid arthritis, or RA, patients on stable doses of methotrexate.
- A 12-week Phase 2 study in ankylosing spondylitis.

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ARRY-162 - MEK for Inflammation Program

MEK has been demonstrated to modulate the biosynthesis of certain pro-inflammatory cytokines, in particular, TNF, IL-1 and IL-6. We believe that the inhibition of MEK will have applications in inflammatory diseases characterized by high levels of these cytokines, such as arthritis, psoriasis and inflammatory bowel disease. ARRY-162 is a first in class, orally-active, selective MEK inhibitor that is active, either alone, or in combination with other agents, in *in vivo* RA models. In Phase 1 clinical trials, ARRY-162 exhibited significant cytokine inhibition and has been well tolerated. We believe ARRY-162 is the only MEK inhibitor currently in development for RA.

Our clinical development activities for ARRY-162 consisted of the following during fiscal 2008:

- Reported Phase 1 clinical trial results in healthy volunteers in June 2008. In that trial, ARRY-162 showed no serious adverse events through 14 days of continuous dosing and significantly inhibited production of the inflammatory cytokines TNF, IL-1 and IL-6, as measured in *ex-vivo*, TPA-stimulated whole blood samples.

- Reported results from a Phase 1b trial of ARRY-162 in combination with methotrexate in stable RA patients. In this study, ARRY-162 showed linear increases in exposure with increasing dose and no drug / drug interactions between ARRY-162 and methotrexate were observed. In addition, ARRY-162 suppressed the production of inflammatory cytokines, relative to methotrexate alone, suggesting that this combination treatment may be more beneficial for patients with RA.

- Completed long-term toxicology studies.

- Initiated a worldwide Phase 2 trial with ARRY-162 added to methotrexate in 200 patients with RA.

We expect to receive top-line results on the Phase 2 RA trial during the second half of calendar 2009.

ARRY 614 - p38/Tie2 for Inflammation and Cancer Program

As discussed above, p38 regulates the production of numerous cytokines, such as TNF, IL-1 and IL-6, the increased production of which can cause inflammation and aberrant tissue proliferation. Tie2 plays an important role in angiogenesis, the growth, differentiation and maintenance of new blood vessels. ARRY-614, an orally active compound that inhibits both p38 and Tie2, has been shown to block angiogenesis, to inhibit inflammation and to antagonize tumor growth, while showing a low side effect profile after prolonged dosing in preclinical models. We believe this compound will have broad therapeutic benefits in various cancers and inflammatory diseases.

During fiscal 2008, we initiated a single and multiple dose escalation study with ARRY-614 in healthy volunteers for safety, tolerability, exposure and inhibition of mechanism-related biomarkers.

During fiscal 2009, we plan to initiate first-in-patient trials in either cancer or inflammatory disease.

ARRY-543 - Pan-ErbB - EGFR / ErbB-2 Program

ErbB-2 and EGFR are receptor kinase targets that are over-expressed in a number of malignancies, including breast, lung, pancreas, colon and head and neck cancers. ARRY-543 is a novel, orally-active dual inhibitor of ErbB-2 and EGFR. It behaves as a reversible ATP-competitive inhibitor with nanomolar potency both *in vitro* and in cell-based proliferation assays.

In preclinical models, ARRY-543 demonstrated significant dose-related tumor growth inhibition when administered orally. It has demonstrated superior activity versus Tykerb® (lapatinib) in most EGFR and ErbB-2 *in vivo* models, equivalent activity to Iressa® (gefitinib)/ Tarceva® (erlotinib) in EGFR models, and enhanced efficacy in certain preclinical models where dual inhibition is relevant when compared to Herceptin® (trastuzumab), Tarceva and Tykerb.

Our clinical development activities for ARRY-543 consisted of the following during fiscal 2008:

- Presented results from a Phase 1 trial of ARRY-543 at the 2007 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics and at the San Antonio Breast Cancer Symposium. ARRY-543 produced prolonged stable disease in patients who have previously failed prior

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treatments with solid tumors. ARRY-543 was well-tolerated up to 400 mg twice daily, or BID, dosing. Systemic concentrations of ARRY-543 increased with escalating doses at all dose levels tested, providing continuous exposure over a 24-hour period. In completed cohorts, sixty percent of patients receiving doses of 200 mg BID and higher had prolonged stable disease. Based on these results, the BID regimen has been chosen for Phase 2 studies.

- Initiated a Phase 1b expansion cohort at the maximum tolerated dose for ARRY-543, with half of the patients with ErbB-2 positive metastatic breast cancer, who had been previously treated with Herceptin, and half of the patients with other ErbB-family expressing cancers.

During fiscal 2009, we plan to initiate two Phase 1b studies of ARRY-543 in combination with Xeloda® (capecitabine) or Taxotere® (docetaxel).

ARRY-520 - KSP Program

ARRY-520 inhibits kinesin spindle protein, or KSP, which plays an essential role in mitotic spindle formation. Like taxanes and vinca alkaloids, KSP inhibitors inhibit tumor growth by preventing mitotic spindle formation and cell division. However, unlike taxanes and vinca alkaloids, KSP inhibitors do not demonstrate certain side effects such as peripheral neuropathy and alopecia.

ARRY-520 has demonstrated efficacy in multiple preclinical cancer models. ARRY-520 caused marked tumor regression in preclinical models of human cancer at tolerated doses, and produced complete responses in two solid tumor models (colon and ovarian) and in leukemia models.

Our clinical development activities for ARRY-520 consisted of the following during fiscal 2008:

- Completed a Phase 1 dose escalation trial in advanced cancer patients.
- Initiated a Phase 1 expansion trial to evaluate the safety, tolerability and preliminary efficacy at maximum tolerated dose.
- Initiated a Phase 2 trial in acute myelogenous leukemia, or AML.

During fiscal 2009, we plan to begin a Phase 2 trial in multiple myeloma.

ARRY-380 - ErbB-2 Program

ErbB-2, also known as HER2, is a receptor kinase target that has been found to be over-expressed in breast cancer and other cancers. Our orally active ErbB-2 inhibitor, ARRY-380, has shown efficacy and a mil