

# QUARTERLY UPDATE

## July 2012 Business Update

### Snapshot

July 16, 2012

AtheroNova Inc. (“AtheroNova” or “the Company”) is a development-stage biotech company creating novel compounds to dissolve or regress atherosclerotic plaque deposits—a thickening of the arteries due to buildup of fat, cholesterol, and other substances. These plaque deposits, which progressively narrow and block the arteries, are the main underlying cause of cardiovascular disease, including heart attack, stroke, and peripheral artery disease (PAD). The Company’s most advanced candidate, AHRO-001, works to significantly reduce the incidence and severity of plaque by employing a bile salt to dissolve existing plaque deposits as well as prevent new ones from forming. Bile salts are an FDA-approved natural compound used to dissolve gallstones. After meeting with the FDA in October 2011, the Company is advancing AHRO-001 into Phase I human clinical trials.



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### Recent Financial Data

Ticker (Exchange)	AHRO (OTC.BB)
Recent Price (07/13/2012)	\$0.90
52-week Range	\$0.45 - \$1.99
Shares Outstanding*	~28.5 million
Market Capitalization	~\$25.7 million
Average 3-month Volume	17,157
Insider Owners + >5%	57.1%
Institutional Owners**	23%
EPS (Qtr. ended 03/31/2012)	\$0.02 (dil.)
Employees	4



\* As of May 8, 2012. \*\* Includes private corporations.

### Key Points

- In July 2012, AtheroNova received a Notice of Allowance from the U.S. Patent and Trademark Office for one of the Company’s main patent applications, which protects its proprietary method of treating atherosclerosis using a bile acid. This represents a key milestone for the Company as it seeks to commence Phase I trials of its lead bile acid-based candidate, AHRO-001, in 2012.
- Lipid regulators, specifically statins, are the most effective method for reducing serum cholesterol levels, achieving blockbuster status with revenues of \$37 billion as of 2010 (Source: IMS Health, Inc.). However, at commonly prescribed dosage levels, they are ineffective at reducing plaque, carry significant drawbacks in their tolerability, and may pose complications resulting from long-term use.
- AtheroNova’s AHRO-001 is being developed to compete with lipid-regulating statins to become the new standard for reducing or eliminating atherosclerotic plaque. In preclinical studies, use of AHRO-001 led to a 95% reduction in innominate arterial plaque formation versus a control group. The compound has not shown morbidity, adverse effects, or mortality and was well tolerated at high doses.
- In late 2011, AtheroNova signed a licensing agreement with Maxwell Biotech Group for AHRO-001, with Maxwell committing to fund Phase I and Phase II human clinical studies in Russia.
- AtheroNova’s management and Board of Directors have experience with many pharma projects (e.g., Botox®, Lumigan®, and Restasis®), and its Scientific Advisory Board includes members from the Cleveland Clinic.
- The Company recently successfully completed preclinical studies with UCLA and Cedars-Sinai, with results to be published in scientific journals for the UCLA study in late 2012 and for Cedars-Sinai by early 2013.

## Milestone: Notice of Allowance Received

In July 2012, AtheroNova achieved a major near-term milestone when it received a Notice of Allowance from the U.S. Patent and Trademark Office (USPTO) for its main patent. A Notice of Allowance entails written communication from the USPTO to AtheroNova that the Company's patent is allowable. It specifies the amount of issue and/or publication fees that are due within three months in order to avoid abandonment of the applications (Source: USPTO). Accordingly, AtheroNova expects to announce the official patent issuance within the next few months once the registration process is complete.

The Notice of Allowance was received for AtheroNova's U.S. patent application #12/024,908 "Dissolution of Arterial Plaque Using Hyodeoxycholic Acid (HDCA)." This patent is key to AtheroNova's continued development efforts, as it protects the Company's method of treating atherosclerosis using a bile acid. AtheroNova has worked toward the issuance of a patent covering the use of HDCA for atherosclerotic plaque lesions for over five years.

The Company has stated that receiving the Notice of Allowance for its "Dissolution of Arterial Plaque" patent supports development of AHRO-001, which is rapidly advancing into Phase I clinical trials. AtheroNova plans to commence Phase I during late 2012.

In addition, with the receipt of application #12/024,908, the Company can move forward with additional pipeline candidates in the AHRO family, as described in its patent applications. For instance, beyond development of AHRO-001, AtheroNova expects to employ its intellectual property to develop multiple pharmaceutical-grade applications for its compounds, potentially in the areas of obesity, hypertension, diabetes, PAD, localized transdermal fat dissolution, and the non-invasive dissolution of lipomas.

## Company Background

AtheroNova Inc. (“AtheroNova” or “the Company”) is a biotechnology company focused on discovering, researching, developing, and licensing pharmaceuticals to reduce or eliminate atherosclerosis—a thickening of the arteries that occurs when fat, cholesterol, and other substances build up in the walls of the arteries and form hardened structures called plaque deposits. These plaque deposits are believed to come from weaknesses or imperfections in the arterial walls or may develop at the site of arterial inflammations. Atherosclerosis is the primary cause of many cardiovascular diseases, including heart attack, stroke, and peripheral artery disease (PAD), with more money spent attempting to treat cardiovascular disease than any other disease or ailment. The condition is so prevalent that cardiovascular disease is the leading cause of morbidity, disability, and mortality in industrialized countries, with atherosclerosis being the primary fundamental pathology.

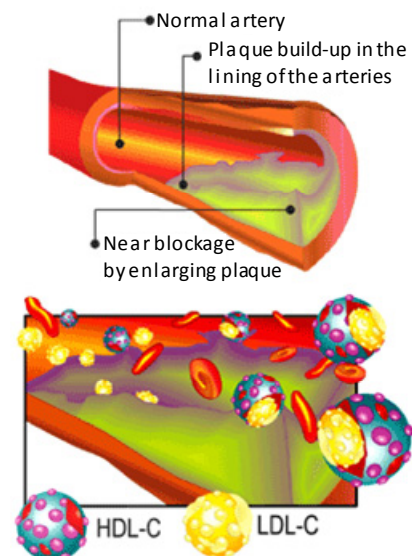
AtheroNova is researching patent-pending applications of bile salts (natural compounds that have been used previously to dissolve gallstones) to regress atherosclerotic plaques (atheromas) via a process called delipidization, which dissolves plaque in artery walls and removes it by natural body processes. The Company’s most advanced compound, AHRO-001, is being developed as a breakthrough regression treatment of atherosclerotic plaque. Using a unique approach, AHRO-001 is intended to dissolve existing atherosclerotic plaques as well as prevent the formation of new ones. The Company seeks to market its product against currently approved therapies, which merely stabilize the disease. It is this potential for plaque regression that AtheroNova believes could distinguish AHRO-001 from other atherosclerosis treatments on the market and candidates in development.

### Formation of Atherosclerosis

Cholesterol deposits or “plaque” accumulate in arteries over time and can be related to diet, heredity, and other blood chemistry factors. Plaque accumulations are the sum of the low-density lipoprotein (LDL) cholesterol that circulates within a person’s blood. It is believed that a higher LDL reading translates into plaque accumulations in the arteries. High-density lipoprotein (HDL) cholesterol is considered the “good” cholesterol and can assist in transporting LDL out of the bloodstream to the digestive system for elimination by the body. This process is illustrated in Figure 1.

Atherosclerotic plaques usually form a protective barrier known as a “fibrous cap,” which may result from inflammation of the arterial wall due to formation of the deposit. The fibrous cap is an attempt by the human body to stabilize the deposit and stop it from abruptly breaking loose. In certain situations, the plaque may rupture regardless and greatly restrict or altogether block blood flow, leading to a heart attack or stroke. If the plaque remains stable, it reduces the available space within the arteries, which restricts blood flow (such as is illustrated in Figure 2 [page 4]). This can result in conditions such as hypertension, kidney failure, macular degeneration, PAD, and erectile dysfunction. There is also evidence to suggest that cognitive impairment may be a sign of reduced blood supply to the brain.

Figure 1  
UNDERSTANDING CHOLESTEROL

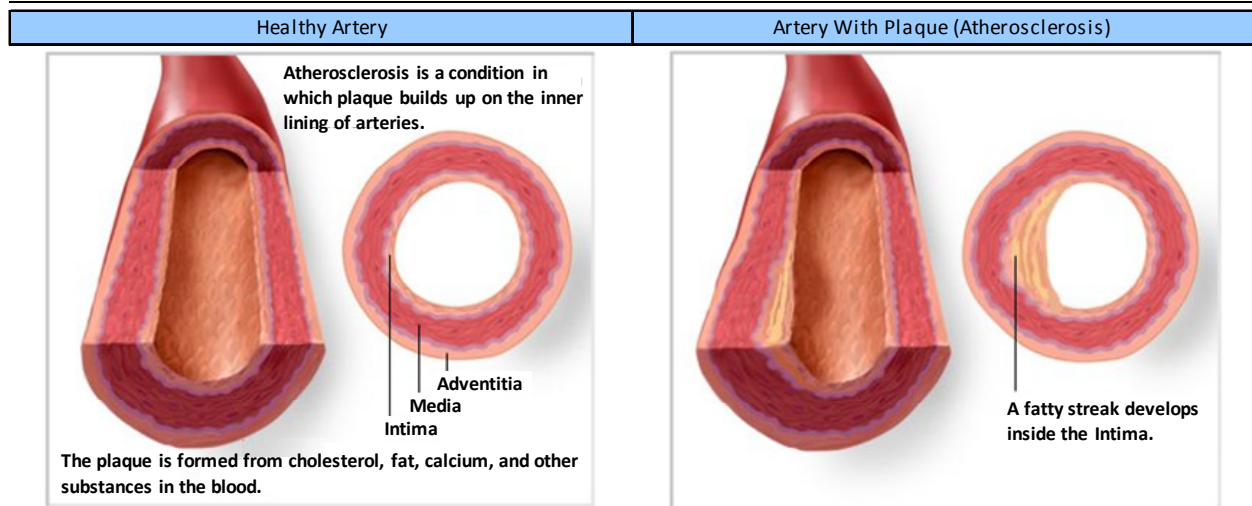


HDL-C (good cholesterol) carry LDL-C (bad cholesterol) away from artery walls. LDL-C sticks to artery walls and can lead to plaque build-up (atherosclerosis)

Source: [www.policosanolprime.com](http://www.policosanolprime.com).

Figure 2

ATHEROSCLEROSIS: HEALTHY ARTERY VERSUS AN ARTERY WITH PLAQUE



Source: American Heart Association, Inc.

### Current Standards of Care

Current atherosclerosis and coronary artery disease (CAD) treatments consist of various therapeutic classes, the most widely prescribed being statins, as well as angiotensin-converting enzyme (ACE) inhibitors, beta blockers (BBs), antiplatelets, calcium channel blockers (CCBs), and nitrates. To date, statins represent the most effective method of reducing serum cholesterol levels, though they are ineffective at reducing plaque. It has long been believed that a patient who exhibits the genetic, dietetic, or disease characteristics prone to plaque accumulations should initially be put on a course of lifestyle and diet changes in order to attempt to control blood cholesterol levels. Smoking cessation, diet, and exercise are thought to be the most important ways an individual can control the balance of HDL and LDL in the body, and thus minimize plaque accumulation. If such measures prove unsuccessful, then the standard course for treatment is a statin, whereby a patient is directed to remain on the drug throughout his/her lifetime. The very nature of statins is to reduce the amount of cholesterol circulating in the bloodstream, which is largely believed to slow or prevent the formation of atherosclerotic plaques—of which cholesterol is a major component. If the statin proves to be ineffective, other measures must be taken. Other treatments for atherosclerosis include drug-eluting stents, catheterization, and balloon angioplasty—though none of these have proven entirely effective at stabilizing or reducing plaque in the arteries.

Significant drawbacks to statins have largely been related to their tolerability in the prescribed dosage as well as the potential complications that can result from long-term use, which may include muscle weakness and pain (which have shown to be the most common), dizziness, headaches, extreme fatigue and flu-like symptoms, diarrhea/constipation, swelling of the ankles, liver dysfunction with elevation of the liver enzymes, neurological problems such as a condition called peripheral neuropathy or polyneuropathy, and total global amnesia, where a patient forgets where and who they are for a few minutes to several hours. These side effects may recede as patients become accustomed to taking the medications.

### ASTEROID and SATURN Studies

AtheroNova has developed its compounds under the premise that atherosclerosis is really a story of largely unsuccessful drug therapies. This is confirmed based on published data from the following studies: ASTEROID and SATURN. The ASTEROID study tested the maximum 40 mg dose of rosuvastatin (AstraZeneca's Crestor®) administered to subjects for two years, demonstrating a 6.7% reduction in plaque. The SATURN study compared the two best-selling statins (Lipitor® and Crestor®) to each other. In a large double-blind, multicenter, randomized trial, it was confirmed that while Crestor® significantly lowered LDL levels when compared to Lipitor®, it was not superior in decreasing atherosclerosis as measured by intravascular ultrasonography (IVUS), which was the primary endpoint. The study did not show a significant difference between the two products in clinical events.

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## Market Size

In 2010, global lipid regulator spending reached \$37 billion, driven by a high prevalence of cardiovascular disease and limited therapeutic options (Source: IMS Institute for Healthcare Informatics' *The Global Use of Medicines: Outlook Through 2015*, 2011). However, the lipid regulator market is expected to decline as the patent protection expiration of atorvastatin (Pfizer's Lipitor®) and rosuvastatin (AstraZeneca's Crestor®) during 2011 and 2012 leads to increased generic competition (Source: Visiongain's *Statins: World Market Outlook 2011-2021*, 2011). In addition, due to the recent regulatory failure of some next-generation therapies, very few new branded products are expected to enter the category in the near term. IMS Health expects the total market for lipid regulators to decline to \$31 billion by 2015 due to lower-cost generics coming to the market. Despite this decline, lipid regulators would still represent the fourth largest therapeutic area behind oncology, diabetes, and respiratory illnesses (Source: IMS Institute for Healthcare Informatics).

## AtheroNova's Pipeline Candidate: AHRO-001

AtheroNova is developing, and seeks to eventually market, a product that could become a new standard of care for patients prone to plaque accumulations. The Company is preparing to enter human Phase I trials to explore the ability of bile salts to dissolve (regress) a statistically significant portion of atheromas in test subjects in a way that is both safe and effective. AtheroNova's most advanced compound in development, AHRO-001, is a bile salt administered via pill or tablet. Through a process called delipidization, the compound is designed to dissolve plaque within the walls of the arteries and, subsequently, safely remove it from the body through natural metabolic processes. The Company is initially targeting individuals with soft vulnerable plaque, as the volume of plaque that one accumulates over a lifetime can remain until death, with no truly effective way to reduce it. AHRO-001 works in a manner that some have likened to liquid Drano® used to unclog drains.

AtheroNova is developing AHRO-001 to directly compete with statins that largely lower cholesterol and stabilize plaque. In preclinical studies, AHRO-001 did not show adverse effects, including morbidity or mortality. Also, it was well tolerated at high doses—something that has been confirmed by other compounds in this family, mainly, ursodeoxycholic acid (also known as UDCA or ursodiol). UDCA, a naturally occurring bile acid and a very close compound to AHRO-001, is used in a drug for gallstone dissolution and is the only U.S. Food and Drug Administration (FDA)-approved drug to treat primary biliary cirrhosis (PBC), with millions of patients taking it without significant side effects.

AtheroNova is conducting additional academic research and has recently completed studies at Cedars-Sinai and UCLA that were successful at verifying plaque and cholesterol reduction as well as safety. Should the Company prove successful in safely and effectively regressing soft, vulnerable plaque via delipidization, it would become the first entity with a proven method to do so and could represent a new treatment for the millions of patients currently seeking to manage their risk for atherosclerosis. As well, AtheroNova could provide new hope to patients who have genetic, dietetic, or disease predisposition to the potentially catastrophic "first event"—where a patient's first atherosclerotic event is a fatal heart attack or stroke.

### *Progression to Commencing Phase I Trials*

In an important milestone, AtheroNova announced in December 2011 that it completed its pre-Investigational New Drug (IND) meeting with the FDA, with the FDA providing guidance on a clear development plan, including Phase I and Phase II protocol outlines. The July 2012 communication from the USPTO allowing AtheroNova's main patent is further fueling the Company's progression into Phase I. The Company is currently incorporating guidance from the FDA and moving forward with its IND-enabling activities.

If successfully approved and marketed, AtheroNova's product candidate could be positioned to address one in three individuals—or greater than 82 million adults (39.9 million men; 42.7 million women)—who have one or more types of cardiovascular disease. As an ultimate goal of ridding the entire body of plaque, the Company conservatively believes that if it is able to regress only 5% with minimal side effects, its product would become a significant disruptive technology.

### **Agreement with Maxwell Biotech Group**

AtheroNova joined forces in 2011 with the Maxwell Biotech Group (<http://maxwellbio.com>), Russia's premier biotech venture capital firm, to license commercialization rights for AHRO-001. Through Maxwell's subsidiary, CardioNova Ltd., this agreement makes Maxwell an equity investor in AtheroNova, committing the Group to fund Phase I and Phase II human clinical studies in Russia. Initial funding of \$900,000 was provided by Maxwell to CardioNova with which to begin Phase I. The license agreement provides for AtheroNova to issue up to \$3.8 million in Common Stock to CardioNova for these studies, to be issued in tranches based on the progress of the studies. Upon successfully developing AHRO-001, CardioNova will be able to commercialize the compound in the territory encompassing the Russian Federation, Belarus, Ukraine, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Moldova, Azerbaijan, and Armenia. In addition, under a separate securities purchase agreement, CardioNova becomes an equity investor in AtheroNova with an initial stock purchase of up to \$267,000, of which \$150,000 has already been invested.

This relationship is important since it secures financial resources to be able to move AHRO-001 to the clinic for Phase I and Phase II studies. As well, it represents AtheroNova's first licensing partnership for AHRO-001 and a significant point for AtheroNova as it completes the preclinical stage of AHRO-001 and the initiation of clinical studies. AtheroNova announced in March 2012 that it commenced the first shipment of AHRO-001 Active Pharmaceutical Ingredient (API) to CardioNova. The clinical-grade material is designated to be used to commence the toxicology studies conducted for Russian regulatory purposes.

In July 2012, CardioNova successfully completed the preliminary Russian toxicology work and is currently preparing final reports for use in Russian regulatory submissions.

### **Agreement with Frontage Laboratories, Inc.**

In April 2012, the Company announced that it had entered into an agreement with Exton, Pennsylvania-based Frontage Laboratories, Inc. (<http://www.frontagelab.com>) to commence work on the formulation, compounding, and tabletization of AHRO-001 in advance of the upcoming Phase I and Phase II human clinical studies. Frontage is one of the leading pharmaceutical contract research organizations (CROs) in the U.S. Under this agreement, Frontage has commenced work on the analysis, formulation, and validation of the various processes and procedures for manufacturing AHRO-001 tablets, and is currently manufacturing the initial formulation of AHRO-001 for use in stability testing.

### **Headquarters and Employees**

AtheroNova is a Delaware corporation formed in 1997, with headquarters in Irvine, California. On May 13, 2010, pursuant to an Agreement and Plan of Merger dated March 26, 2010, a subsidiary, Z&Z Merger Corporation, merged with and into Z&Z Delaware and the surviving subsidiary corporation changed its name to AtheroNova Operations, Inc. As of March 9, 2012, AtheroNova had two full-time employees and two contract employees.

## Key Points to Consider

- AtheroNova Inc. has developed intellectual property for a class of compounds with the potential to reduce the incidence and severity of atherosclerosis—a disease in which the buildup of cholesterol, fats, or other fatty substances in and along the walls of arteries causes thickening, hardening, and blockage. Atherosclerosis is the main cause of cardiovascular disease.
- Regression and stabilization of atherosclerotic plaque could become a new standard for treating patients with cardiovascular disease. Current standards of care, such as statins, represent the most effective method to date for preventing atherosclerosis. However, at commonly prescribed dosage levels, statins are ineffective at reducing plaque and carry significant drawbacks related to their tolerability. Furthermore, complications can result from long-term use. Other standards of care, including drug eluting stents, catheterization, and balloon angioplasty, do not reduce plaque volume.
- In the U.S., there are roughly 82 million individuals presenting with some form of cardiovascular disease, supporting a \$37 billion U.S. market for lipid regulators (as of 2010).
- AtheroNova seeks to become the standard for reducing or eliminating atherosclerosis. The Company's most advanced product candidate, AHRO-001, works to significantly reduce the incidence and severity of plaque by dissolving existing atherosclerotic plaque deposits and removing them by natural body processes (via a method called delipidization) as well as preventing the formation of new plaque deposits.
  - AHRO-001 has not shown morbidity, adverse effects, or mortality in preclinical proof of principal and mechanism of action studies and is well tolerated at high doses.
  - Initial preclinical study data conducted at UCLA's David Geffen School of Medicine showed that following exposure to AtheroNova's AHRO-001, mice with very high levels of plaque had a 95% reduction in the amount of innominate arterial plaque versus the control group. On the safety side, all blood tests for the group that was given AHRO-001 demonstrated no toxicity. These findings were presented at the 2011 American Heart Association (AHA) Scientific Sessions in Orlando, Florida.
- The FDA has approved bile salts as a pharmaceutical therapy to dissolve gallstones in certain patients. Such treatments have been well tolerated and have a history of safety and efficacy. Accordingly, AtheroNova believes that the established safe administration of these natural compounds provides its bile salt-based therapeutic with a precedent for a positive safety and efficacy profile.
- Only one currently available statin, rosuvastatin (Crestor®) by AztraZeneca PLC (AZN-NYSE), has been able to show statistically significant measurable regression of atherosclerotic plaque in coronary arteries. According to AtheroNova, these results were achieved on patients taking the maximum approved dosage for two years.
- AtheroNova signed a binding term sheet in September 2011 with the Maxwell Biotech Group related to commercialization rights for AHRO-001, whereby Maxwell committed to fund Phase I and Phase II human clinical studies of AHRO-001 in Russia in return for up to \$3.8 million in Common Stock and an exclusive license to develop and commercialize AHRO-001 in select territories within the Russian Federation and other former Soviet Republics. Also, the Company entered into an agreement with Frontage Laboratories, Inc. to commence work on the formulation, compounding, and tabletization of AHRO-001 in advance of the upcoming Phase I and Phase II human clinical studies. The first shipment of AHRO-001 Active Pharmaceutical Ingredient (API) took place in March 2012 for use in toxicology studies for Russian regulatory submission purposes.
- Beyond developing AHRO-001, AtheroNova plans to employ its IP to develop multiple pharmaceutical-grade applications for its compounds, potentially in the areas of obesity, hypertension, diabetes, peripheral artery disease (PAD), localized transdermal fat dissolution, and the dissolutions of lipomas.

- In June 2012, the Company entered into an Amendment Agreement with the holders of its senior convertible debt. Under the Amendment, the Company's option to call an additional \$1,500,000 of Notes was extended for 60 days and the qualifying factors were amended. The Notes were also amended to remove anti-dilution clauses and added an automatic conversion clause upon qualification for a national exchange listing.
- In July 2012, the Company received a Notice of Allowance for its primary patent application for the dissolution of arterial plaque. AtheroNova has additional patents pending for other applications for its compound.
- AtheroNova's management possesses extensive experience in the healthcare and pharmaceutical spaces, both at established companies as well as successful start-up biotechnology ventures. The Company's leadership has helped in the development, regulatory approval, worldwide registration, and commercialization of several therapeutic compounds and devices.
- As of March 31, 2012, AtheroNova held over \$276,000 in cash.



## Risks

Some of the information in this Quarterly Update relates to future events or future business and financial performance. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in AtheroNova's statements on Forms 10-K, 10-Q, and 8-K, as well as other forms filed from time to time. The content of this update with respect to AtheroNova has been compiled primarily from information available to the public released by the Company through news releases, Annual Reports, and Securities and Exchange Commission (SEC) filings. AtheroNova is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by AtheroNova. Certain summaries of activities have been condensed to aid the reader in gaining a general understanding. For more complete information about AtheroNova, please refer to the Company's website at [www.atheronova.com](http://www.atheronova.com). Additionally, please refer to Crystal Research Associates' base report, the Executive Informational Overview® (EIO) dated June 6, 2012, and located on Crystal Research Associates' website at [www.crystalra.com](http://www.crystalra.com) for more comprehensive details of AtheroNova's risk factors.

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# Crystal Research

a s s o c i a t e s

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