

# BioCentury

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## *Emerging Company Profile*

### Altair: Breathing easier with antisense

By Erin McCallister  
Senior Writer

Several compounds in development to treat asthma have been designed to modify the underlying disease by inhibiting or disrupting the inflammatory activity of the cytokines IL-4 and IL-13. So far, compounds targeting one or the other have been unsuccessful. But **Altair Therapeutics Inc.** thinks it can shut down the inflammatory pathway by targeting a subunit that is shared by the receptors for both cytokines.

The biotech, which was spun out of **Isis Pharmaceuticals Inc.**, also believes its lead antisense compound will allow for better dosing than other inhibitors of the same target. AIR645, an antisense molecule targeting the IL-4 receptor subunit alpha mRNA, is in Phase IIa testing, with data expected in 3Q10.

There are three subunits in each of the IL-4 and IL-13 receptors, including the shared IL-4 receptor subunit alpha. IL-4 and IL-13 signal through this subunit and trigger the JAK/STAT pathway in inflammation, leading to activation of neutrophils. Neutrophils have been implicated in lung damage.

According to President and CEO Joel Martin, compounds that inhibit IL-4 or IL-13 alone have been unsuccessful because they did not completely shut down the pathway, resulting in a lack of efficacy.

#### Altair Therapeutics Inc.

San Diego, Calif.

Technology: Inhaled antisense molecule targeting IL-4 receptor (CD124) subunit alpha

Disease focus: Inflammation

Clinical status: Phase IIa

Founded: 2007 by Susan Gregory and Pratik Shah

University collaborators: None

Corporate partners: None

Number of employees: 7

Funds raised: Not disclosed

Investors: Domain Associates, Age-Chem Venture Fund, Thomas McNerny & Partners and Forward Ventures

CEO: Joel Martin

Patents: 1 issued covering lead compound AIR645

“The asthma pathway is regulated by IL-4 and IL-13, and there is considerable redundancy between the two pathways, so it is not enough to knock out just one. But both cytokines rely on a common subunit — IL-4 receptor alpha — and it turns out if you block that, you block the signaling,” Martin told BioCentury. “If the protein is not made, the subunits cannot

come together in the correct conformation at the cell surface, and you don’t get the signaling.”

Altair is not the only company targeting IL-4 receptor subunit alpha. Aerovant, a recombinant human IL-4 variant from **Aerovance Inc.**, is in Phase IIb testing. **Amgen Inc.** is developing AMG 317, a mAb that completed a Phase II trial in asthma in 2009.

But Martin believes AIR645, which is delivered via inhalation, will have advantages in safety, dosing frequency and route of administration.

“We have a heavily modified single-stranded molecule that is designed to avoid inflammatory reactions, and we are delivering directly to the organ of interest with low systemic exposure,” he said.

Data from a Phase I trial in healthy volunteers and patients with mild asthma showed dose-dependent exposure in the sputum. Moreover, concentration in sputum that was more than 1,000 times higher than concentration in plasma. The lower plasma concentrations indicate reduced systemic exposure, which could mean a safer compound.

AIR645 has a phosphorothioate modification that allows for better tissue distribution and a methoxyethyl modification that increases the hybridization affinity for the target mRNA and provides better

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**Altair,**  
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potency and safety. According to Martin, these modifications translate into a longer half-life for AIR645 and reduced dosing frequency.

“We think we can dose as low as once per week,” he said.

In the Phase I trial, AIR645 had a sputum half-life of about five days. Altair has not disclosed the exact dosing regimens in its Phase IIa trial. According to [clinicaltrials.gov](http://clinicaltrials.gov), the regimens range from a maximum dose frequency of once per day, to up to six doses in 22 days.

Aerovance’s Aerovant was tested using a twice-daily regimen, while AMG 317 has been tested as a once-weekly subcutaneous injection. Martin believes an inhaled once-weekly asthma treatment will be preferred.

“AIR645 is given with a nebulizer, which is a very familiar setting. You have to be pretty severe to be interested in getting injections on a regular basis,” he said.

With mAbs, there is a risk that patients will develop neutralizing antibodies, which Martin suggested could lead to anaphylaxis. Neutralizing antibodies were seen in 17 patients (7.8%) in the AMG 317 arm of Amgen’s Phase II trial, but no serious adverse events were reported.

Altair is open to partnering AIR645 at any point in development, but also is prepared to go it alone. Martin said the biotech also is likely to develop the compound for additional, undisclosed indications.

Isis granted Altair an exclusive license to AIR645 as part of its spinout in 2007. Isis has focused its internal efforts on cardiovascular and metabolic diseases.

Altair closed a \$17 million extension to a series A round in November. The total amount raised was not disclosed.

#### COMPANIES AND INSTITUTIONS MENTIONED

**Aerovance Inc.**, Berkeley, Calif.

**Altair Therapeutics Inc.**, San Diego, Calif.

**Amgen Inc.** (NASDAQ:AMGN), Thousand Oaks, Calif.

**Isis Pharmaceuticals Inc.** (NASDAQ:ISIS), Carlsbad, Calif.