

# >>>GAGs - a drug development program targeting allergic inflammatory diseases, particularly allergic rhinitis, asthma and eczema

## >>>market opportunity

*Allergic Rhinitis* affects about 20% of the US population and some 15% of the worldwide population. Approximately 20% of allergic rhinitis patients also have symptoms of asthma.

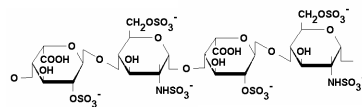
*Asthma* is the most common childhood chronic disease, whose prevalence is increasing. It affects some 155 million people world-wide, with mortality rates in the range of 1 to 5 persons per 100,000 population.

The incidence of *Eczema* has increased 2 to 3 fold in the last thirty years. About 20% of children and 1% to 3% of adults in Western countries suffer from some manifestation of this disease.

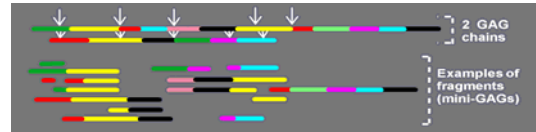
Prescription sales for allergic rhinitis drugs were just under US\$6 billion in 2001, with total sales being approximately US\$10 billion in the same year. Market growth has averaged 15% per year since the early 1990s. Sales of anti-asthmatic products are currently approximately US\$3 billion per year. Recently introduced new drugs have enjoyed very rapid market penetration. In short, the addressable markets are huge and respond quickly to the introduction of new drugs which prove efficacious.

## >>>project description

Heparin/heparan sulphate glycosaminoglycans (GAGs) are an important subset of complex polysaccharides, and represent an under-exploited third major class

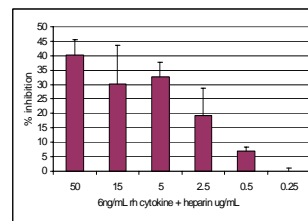
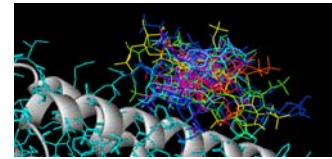
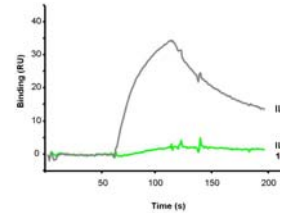


of biological polymers, along with nucleic acids and proteins. Recent understandings of GAG biosynthesis, structure and function now create the opportunity to capitalise on the large structural diversity of GAGs in drug discovery programs. Extensive clinical experience with various heparin products and a good understanding of its toxicity (mainly anticoagulant properties) suggests that GAG-based drugs can be developed and will be well tolerated. There are now precedents to demonstrate that compounds of this type can be successfully synthesised economically and in commercial quantities.



The GAGs Program has:

- Generated a library of miniGAGs using chemical and enzymatic cleavage techniques.
- Identified novel active GAGs using in-vitro binding assays (BIAcore) and tissue culture assays.
- Identified novel GAGs derived from heparin and heparan sulphate that bind to validated asthma, allergy and inflammation targets.
- Demonstrated target protein dependent biological activity is inhibited by novel miniGAGs in a dose dependent fashion. ID50 observed for specific GAGs are at a sub  $\mu$ M level.
- Identified GAG binding sites on key proteins.



With a target of having a drug candidate ready for Phase I clinical trials by Q4 2008, next steps will go from completion of a proof of concept study

using human nasal polyps *ex vivo* and a validated animal model, through lead optimisation, candidate selection and a formal pre-clinical drug development and toxicology program.

## >>>target product profile

The therapeutic endpoint goal for the GAGs Program is to obtain new chemical entities which will be at least as efficacious as inhaled corticosteroids and, in longer term use, more efficacious than non-drowsy anti-histamines in the treatment of chronic allergic rhinitis, but without the side-effects that render corticosteroids unsuitable for long-term administration.

Other features of the TPP include inhaled delivery, once per day administration, fast onset and long duration of action and suitability for combined therapy with corticosteroids.

### >>>competing technologies

Inhaled corticosteroids (ICS) or Intra-nasal corticosteroids (INCS) are effective for most patients but there appears to be a reluctance by patients to use this type of therapy due to a perception about serious side effects. These are caused because corticosteroids affect a large range of different proteins – they are not disease specific. Steroid-sparing practices/therapies are certainly marketable.

Anti-histamines are not effective against the congestion associated with chronic allergic rhinitis and many, even the 2nd generation drugs, may induce drowsiness.

Omalizumab, the anti-IgE antibody, is a relatively new therapy. It is primarily used as add-on therapy to ICS because it does not improve airway responsiveness and has modest efficacy. The dose constraints and delivery mechanism (subcutaneous injection) are an added disadvantage. Studies suggest it is not cost effective.

A number of new therapies are in various stages of development and trial. High cost, low efficacy, side effects and mode of delivery create problems for most of these.

There is a market opportunity for a safe, inexpensive therapy which acts quickly and is long lasting and which is as effective as corticosteroids and/or can be used to significantly reduce the need to use corticosteroids.

### >>>market entry

All intellectual property is owned by Curtin University of Technology and handled by the Western Australian Biomedical Research Institute. Alternatives for development will be considered to advance the technology. For example, should a new corporate entity be established all intellectual property will be assigned across. Alliances will be developed with organisations to add value to the opportunity.

### >>>intellectual property

An International Patent Application, "Therapeutic Agents and Uses Therefor", is at the PCT stage with a priority date of 19 April 2004. The application covers:

- GAG binding sites on target proteins.
- Novel structures which have been demonstrated to bind two target proteins.
- Compound structures, not necessarily involving GAGs, which bind two target proteins.
- A semi-synthetic approach to the production of heparin-like fragments that bind the target proteins for use as therapeutics.

### >>>further information

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