



INVION

Targeting inflammation



Dear Shareholder,

I am very pleased to provide this update covering Invion's programs and operations.

The first half of 2016 has been important for the company on a number of levels.

Activities directed towards further progression along the development pathway for INV102 (nadolol) commenced with Invion's meeting in March with the US FDA to discuss Phase 3 plans for oral nadolol.

Shortly thereafter, we received a Notice of Allowance for the smoking cessation patent in the People's Republic of China.

Also in March, Van Leeuwenhoeck Research (US) published their updated research – Into Higher Gear – which can be found at Invion's website.

Following this, in May, we presented data from the largest clinical trial the company has completed to date - the Phase 2 trial of oral INV102 (nadolol) in patients seeking to quit smoking - to the Annual Meeting of the American Thoracic Society.

As shareholders are aware, following the completion of major development milestones in all four current programs in late 2015, the company's focus has been on activities aimed at realising value for one or all of the company's three drug assets.

Our position is that while nadolol has historically been used to treat migraine and high blood pressure, we know that it also blocks the beta-arrestin pathway, which is strongly implicated in the phenotype of chronic airway disease. Blocking this pathway and reversing abnormal mucus production offers a promising and novel method of treating an underlying cause of chronic airway diseases including asthma, COPD and cystic fibrosis.

Therefore, in parallel with the above accomplishments, we have been working through a comprehensive program of business development and partnering activities.

We have also reduced overhead to minimise burn and preserve capital while business development activities continue.

More detail on all of the above can be found in the following pages.

We continue to be driven to realise value for the company's assets through a sale, licencing or partnering transaction, and I look forward to keeping you informed of progress in the coming period.

Yours faithfully,

Dr Greg Collier
Interim Executive Chair

INVION LIMITED (ASX:IVX) INVESTOR UPDATE

July 2016

Highlights:

- ✓ **Activities in 1H 2016 have focused on progression on clinical development pathway for oral INV102 (nadolol) with a successful meeting held with the FDA, presentation of Phase 2 smoking cessation data to the American Thoracic Society, and receipt of Notice of Allowance for smoking cessation patent in China**
- ✓ **Business activities remain focussed on partnering and/or licencing one or all of the company's three drug assets**
- ✓ **Company continues to reduce overheads to minimise burn and preserve capital**



Meeting with the FDA for INV102 (nadolol)

In March, Invision's Dr Mitchell Glass, and Dr Mario Castro, Professor of Medicine and Pediatric at Washington University School of Medicine (St Louis), met with the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) of the FDA to discuss Phase 3 plans for development of oral nadolol as a treatment for patients with COPD who cannot quit cigarette smoking.

The company and the FDA engaged in a productive dialogue on the design and regulatory target of the Phase 3 plan for oral nadolol, and Invision team members were able to explain to senior FDA officials the role that airway healing can play in enabling these patients to quit, by reducing cough and phlegm. Importantly, Invision was able to place the smoking cessation program into the context of treating COPD.

Notice of Allowance – China patent for smoking cessation

Also in March, we were pleased to receive notification of allowance on the patent right for the use of beta-adrenergic inverse agonists for smoking cessation, from the State Intellectual Property Office of the People's Republic of China.

Chronic respiratory diseases are the second leading cause of death in China, with tobacco

smoking, air pollution and biomass fuel use being the major drivers. China has one of the world's highest rates of smoking, with approximately 320 million people or a quarter of the world's smokers. One in six tobacco-related deaths worldwide occur in China.

The use of beta-adrenergic inverse agonists for smoking cessation is the second family of core patents for oral nadolol. Claims in this patent family are directed to the use of beta-adrenergic inverse agonists for the prevention of mucus hyper-secretion.

The United States Patent and Trademark Office (USPTO) acting as Patent Cooperation Treaty (PCT) International Preliminary Examining authority, has previously issued a notice that all claims under this patent application meet PCT requirements for industrial applicability, novelty and inventive step.

This patent family provides an important layer of protection for the future development and commercialisation of nadolol within the People's Republic of China where we believe that it has specific application as a novel treatment for smoking cessation and broad potential for use in a range of chronic airway diseases.

Phase 2 data presented to the American Thoracic Society

In May, Invision presented data from its Phase 2 clinical trial of oral nadolol to the Annual Meeting of the American Thoracic Society (ATS).

The presentation outlined that in research by collaborators, INV102 (nadolol) has been shown to uniquely and specifically block the beta arrestin pathway of beta 2 receptors on airway epithelial cells; to prevent or treat goblet cell hyperplasia and mucous metaplasia in animal models of obstructive airway disease; to act effectively when delivered to animals by inhaled route at 1/1000 of the oral dose; and to decrease airway hyper-responsiveness in mild persistent asthma in Phase 2 clinical trials.

The key points of the presentation were that nadolol was safe and well-tolerated in the treated population of patients who trying to quit smoking (having been previously unable to quit); that 62/ 69 patients achieved full dose of 100mg/day of nadolol; that, positively, there was no differentiation in the safety profile of patients treated with nadolol versus placebo; and that, critically, data showed a statistically significant improvement in mucus protein **MUC5AC** v placebo, which rebounded after drug cessation.

Further, Drs Glass and Castro discussed with delegates that the study had shown a trend towards reduction in daily cigarette use that would translate from a pack per day to less than 2 packs per week over 8 weeks, and that the study supports a next study either in smoking cessation or the treatment of the broader population of patients with chronic bronchitis.

We were very pleased to have the abstract accepted and to have been able to present to the ATS - there are very few medications that help smokers quit, and we believe that nadolol represents a potential major advance for them.

INV102 (nadolol) in mild asthma

As shareholders know, in a separate study funded by the NIH, Invion is examining the effect of nadolol in patients with mild asthma.

As targeted, this Phase 2 investigation of 66 patients enrolled across three sites in the US completed dosing in 1H 2016, and we anticipate data from this study in the coming months.

The clinical, biomarker and biopsy data from this study, taken with the data from the Phase 2 smoking cessation study, should present a much clearer picture of the impact of nadolol on airway diseases.

INV104 (zafirlukast)

As investors will know, Invion's collaboration with Hovione is designed to bring the first inhaled, dry powder version of zafirlukast to market using Hovione's proprietary inhalation hardware technology.

We expect that delivery of this non-steroidal drug in this way will provide superior benefit and bypass any problems currently associated with systemic delivery.

Hovione's critical work on formulation and manufacturing has meant we have continued to make good progress along the development path to become toxicology and Phase 1 ready.

INV103 (ala-Cpn10)

We continue partnering discussions for our third asset, INV103, the naturally occurring human protein was most recently the focus of a Phase 2 study in patients with the autoimmune disease, lupus.

Operations

In late 2015, Invion completed all projected R&D activities on its three drug assets across four development programs, and subsequently appointed Ferghana Partners Group for a period of six months to increase our reach and progress various potential commercial opportunities. We now continue to actively pursue a number of these introductions and discussions.

As previously reported, in 2Q 2016, following the meeting with the US FDA regarding the smoking cessation program for nadolol, and reflecting the reduced R&D and operational activity while business development activities continue, the company reduced headcount to further reduce burn and preserve capital during this interim phase for the company.

In the current quarter, the company will lodge and expects to receive an R&D tax cash rebate against local and overseas R&D activities conducted in the 2016 financial year. We believe that this cash rebate combined with cash on hand and substantially reduced operating outflows, will see the company continue operations without the need to raise further capital in the near term.

Now and Next

The strategy continues to be the realisation of value for one or all of the company's assets, via a commercial transaction or partnership.

Invion is a life sciences company focussed on the development of treatments for major opportunities in respiratory and autoimmune disease.

Invion has three drug assets in development across four development programs:

INV102 (nadolol) is a beta adrenergic biased ligand targeted to reverse mucous metaplasia in the airway epithelium treat chronic inflammatory airway diseases. In Q4 2015, Invion reported that data from a 155 patient phase 2 study of oral INV102 in smoking cessation demonstrated good safety and that treated patients were more likely to stop smoking completely or dramatically reduce the number of cigarettes smoked. Feasibility for an inhaled version of the drug to potentially treat COPD and cystic fibrosis is well-progressed with 3M Drug Delivery Systems, and toxicological studies have commenced. In addition, a phase 2 study of oral INV102 in mild asthma patients funded by the US NIH is fully recruited and completed dosing in 1H 2016, with data anticipated 2H 2016.

INV104 (zafirlukast) is a leukotriene receptor antagonist (LTRA) that reduces inflammation, constriction of the airways, and the build-up of mucus in the lungs. An FDA-approved oral therapy, Invion is, through a joint development and licensing agreement with Hovione Scientia Limited, developing a proprietary dry powder formulation of the drug for the development of INV104 (zafirlukast) as a potential inhaled therapy for asthma.

INV103 (ala-Cpn10) is a modified, naturally occurring human protein which has been proposed as a founding member of the Resolution Associated Molecular Pattern (RAMPs) family hypothesised to maintain and restore immune homeostasis. Invion reported final data from its phase 2 clinical trial in lupus patients in Q3 2015. 30mg and 100mg iv twice weekly showed reduced response to stimulation by LPS after 1 month of dosing. These data, which reflect relevant activity at the target cell type in patients with a target (autoimmune) disease, has formed the foundation of partnering discussions for this program.

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