Actinogen LIMITED
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31 July 2014
ASX Release

Actinogen Limited (ASX: ACW)

June Quarter Appendix 4C & Commentary

The Board of Actinogen Limited (ASX: ACW) would like to update the Company's shareholders and the market on its activities over the last quarter.

Cancer Stem Cell Stem Project

One of Actinogen's lead therapeutic programs is focused on discovering and developing drugs to treat brain cancer and potentially other oncological diseases by the targeted killing of cancer stem cells (CSCs). In February the Company announced it had entered into a research agreement with Curtin University to conduct further studies on the Company's CSC Project.

Cancer stem cells have been reported in many human tumours and are classified as a highly tumorigenic subpopulation that drives tumour formation, proliferation and metastasis. CSCs share a variety of biological properties with normal stem cells such as capacity for self-renewal and propagation of differentiated progeny. However, CSCs differ from normal stem cells in their inherent resistance mechanisms against radiation- and chemotherapy-induced cancer cell death, enabling them to survive and initiate tumour recurrence. Despite their potential clinical importance, the regulation of CSCs at the molecular level is not well-understood and no drugs specifically targeting CSCs have been developed to date. However, recent research in brain tumours has identified a CD133+ cell population as a cancer stem cell population, giving the way to some targeted therapeutic approaches.

In its previous experiments Actinogen have tested a total of 11 actinomycetes' supernatants against U87MG and U125MG neurospheres (free floating clusters rich in stem cells). The results have demonstrated that two isolates killed the whole cell population (ACN 5059 and ACN 5086). Cells which had died due to supernatant treatment had a high percentage of CD133+ cells, and thus actinomycete isolates ACN 5059 and ACN 5086 can be assumed to target CD133+ cells.

Currently, Actinogen and Curtin University are examining the effects of actinomycete isolates on cell viability in four different GBM (glioblastomamultiforme, a type of brain tumour) cell lines (U138, U87, A172 and LN18) using additional new techniques and assays. To confirm the activity is specific against cancer stem cells, the cells were grown in conditions that provide for the development of sphere formation. Identification of CSCs within these cultures was based upon the presence of the cell surface markers CD133 and CD44. The isolates were then tested on their ability to induce cell death in cultures enriched with CD133 and CD44 positive cells.

The first study was conducted in the laboratory of Professor Arun Dharmarajan using methodologies established by his research group. The results demonstrated substantial reduction of proliferation in CSC populations in GBM cell lines (A172, U138, U87, U373). In addition, CSC sphere disruption, cell anchorage, and cell death were observed with different isolates for the CSCs across all four cell lines. This data is consistent with our previous internal results and supports the strong anti-cancer activity of some of the actinomycetes isolates.

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Professor Dharmarajan is among world leading scientists in the area of cancer stem cell research and is a discoverer of secreted frizzled-related protein 4 (sFRP4) that was recently shown to inhibit cancer stem cell proliferation in several tumours including the brain (Warrier et al (2014), Oncology Research, 21(2), 93-102).

Antibiotic Research Project

The Company continues its focus on drug development via its Antibiotic Research Project; with its scientific team currently conducting trials at its new laboratory premises at Murdoch University's State Agricultural Biotechnology Centre (SABC), Western Australia.

Antibiotic-resistant bacteria are becoming an increasing global problem, with much research and investment directed to discovering new effective agents and treatment modalities. Infections caused by resistant microorganisms often fail to respond to the standard treatment, resulting in prolonged illness and greater risk of death. The death rate for patients with serious infections treated in hospitals is about twice that in patients with infections caused by non-resistant bacteria. A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRE) and *Clostridium difficile*.

The Company has identified the importance of continuing the research in this field due to the global demand for new potential agents and on the back of positive initial results conducted on numerous strains of bacteria, in particular MRSA and VRE.

Actinogen owns a private existing database of over 6000 actinomycetes. Previously, the library has been screened to identify actinomycetes able to produce compounds with antimicrobial activity against resistant strains. The actinomycetes are then tested for activity against the MRSA panel, VRE, *Candida spp*., *Pseudomonas aeruginosa* and the anaerobic pathogen *Clostridium difficile*.

These testing panels consist of clinical isolates of microorganisms that have developed serious antibiotic resistance patterns and can therefore be used to increase the likelihood of finding new antibiotics.

Actinogen employs a series of screening tests which become more stringent. Primary screening is a rapid test to detect the production on solid agar of an isolate producing an antibiotic directed to one or more of the test organisms outlined above. Secondary screening is then carried out on known antibiotic producing isolates, in liquid culture. Once actinomycetes with antimicrobial activity against the clinical test isolates have been identified, Actinogen then tries to identify the active compound from public literature and databases. If the compound cannot be matched to an existing substance, it is sent to an independent laboratory to obtain a molecular structure.

In the Actinogen library 69 isolates have shown activity against the entire MSRA panel, 11 isolates have shown activity against the entire *Candida spp*. panel and 58 isolates have shown activity against VRE. Each compound with activity against the MRSA panel and *Clostridium difficile* has the potential to become a new antibiotic; however extensive further testing is required in order for this to be established.

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The research team has currently inoculated the previously identified isolates and is currently retesting these for activity against MRSA, *Candida spp.* and *C. difficile*, with initial results expected by the end of the third quarter 2014. Of particular interest are the antimicrobial actinomycete isolates that produce unidentifiable active compounds. Future work will include isolating and testing the active compound using HPLC and fraction collection. If the isolation of the active compound is successful, it may be sent to an independent laboratory for further characterisation.

Collaborative and Royalty Agreement with Leaf Energy Ltd (ASX: LER)

On 23 December 2013, the Company announced that it had signed a Collaborative and Royalty Agreement with ASX listed company Leaf Energy Ltd, where LER will fund the further studies in the Company's Bioethanol Project; in which the Company previously identified strains of actinomycetes capable of producing cellulase(s). Cellulase(s) are enzymes used to breakdown cellulose from plant material, papers and industrial waste glycerols (Biomass), and are an important step in the production of second generation bioethanols.

The traditional method of producing cellulases is very costly and requires significant capital for infrastructure, requiring an anaerobic and high temperature and pressure environment ACW's can produce cellulases in an aerobic environment at low temperature and pressure and at significantly lower costs

ACWs enzyme production method is complimentary to LER's Glycerol Pre-treatment Process which uses cheap, recyclable glycerol at low temperature and pressure, in a simple and highly effective process

The trials currently being conducted by the Company's scientific team, and in collaboration with LER's scientific advisors; is in an advanced stage with initial results expected by the end of the third quarter 2014.

On completion of LER's fully funded initial trial, LER will have the option to contribute further funding towards additional trials to explore the potential synergy of other actinomycetes in the Company's library. The Company will grant LER the rights to exclusive uses of any of the methods of production solely developed as part of the collaborative process in return for a net profit royalty on LER's future licensing arrangements.

The potential market opportunity is very large, with LER's Glycerol Pre-treatment process requiring a fracture of the costs and infrastructure to current worldwide methods and processing facilities, having a highly scalable business model with licensing into multiple territories and markets, and providing for excellent environmental credentials with large carbon savings.

Salt Tolerance Project

Actinogen has been approached by third parties expressing interest in the Company's salt tolerant actinomycetes project. Actinogen has been screening actinomycetes from its existing database and testing them to see if they have any ability to survive in salty environments. The aim of this research is to develop a product that will help farmers and other plant producers grow plants and crops in salt affected environments, which is a growing problem worldwide and in particular within Australia.

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Recent screening shows encouraging results identifying four isolates that can tolerate 10% saline, have the potential to survive in high salt environments and continue to lead to the production of humus to aid in the re-establishment of salt tolerant plants and the rehabilitation of salt affected soils.

The Company has entered into a non-disclosure agreement with a party of interest to further explore the synergies with their existing projects with the potential for commercial collaborations.

Shikimic Acid Project

In July 2012, Actinogen discovered that it could produce shikimic acid from certain actinomycetes. This shikimic acid has been produced on a molecular level only and not yet on a scale sufficient to commercialise the project. Shikimic acid is the main (and one of the most expensive) components used to produce the influenza medication, Tamiflu. Actinogen's method for the production of shikimic aid is different from and potentially cheaper than, the current processes of producing shikimic acid currently be utilised by the primary manufacturers such as Roche. The Company is continuing to explore collaborative opportunities in this area.

-end-

Dr Brendan de Kauwe
Executive Chairman
Actinogen Limited

About Actinogen Limited
Actinogen Limited (ASX: ACW)

Actinogen is dedicated to the discovery and isolation of a group of environmental bacteria known as the Actinomycetes. Actinomycetes have been shown to be able to use a wide range of unusual nutritional resources and often produce bioactive molecules as a by-product that have been proven to be useful to man; including well known commercial examples such as bacterial antibiotics, anticancer agents and a variety of other chemicals that are used in the control of physiological and physical processes.

The Company's primary focus is on drug development and therapeutics, with one of its lead therapeutic programs directed towards discovering and developing drugs to treat brain cancer and potentially other oncological diseases, by the targeted killing of cancer stem cells (CSCs); with research currently being conducted in collaboration with Curtin University.

In addition, there are examples of Actinomycetes that can degrade industrial wastes such as oils, tar, domestic and industrial waste, and the rehabilitation of oil spills. The Company is currently conducting research in the breakdown of Biomasses to Bioethanols in collaboration with Leaf Energy Ltd (ASX: LER).

Actinogen has proven high-level expertise in the discovery and isolation of Actinomycetes from WA soils and in the detection of bioactive molecules they produce. The Company's strategy is to collaborate with groups nationally and internationally who are active in the development of technology that is synergistic with or that could utilise the Company's current Actinomycetes research projects and exclusive intellectual property.

Rule 4.7B

Appendix 4C

Quarterly report for entities admitted on the basis of commitments

Introduced 31/03/00 Amended 30/09/01, 24/10/05, 17/12/10

Name of entity

ACTINOGEN LIMITED

ABN	Quarter ended ("current quarter")
14 086 778 476	30 June 2014

Consolidated statement of cash flows

	Cash flows related to operating activities	Current quarter $A'000	Year to date (12 months) $A'000
1.1	Receipts from customers	-	20
1.2	Payments for		
	(a) staff costs	(13)	(56)
	(b) advertising and marketing	-	-
	(c) research and development	(90)	(269)
	(d) leased assets	-	-
	(e) other working capital	(20)	(148)
	(f) corporate reconstruction costs	-	(90)
1.3	Dividends received	-	-
1.4	Interest and other items of a similar nature received	7	14
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Other (R&D tax rebate)		147
	Net operating cash flows	**(116)**	**(382)**

+ See chapter 19 for defined terms.

		Current quarter $A'000	Year to date (12 months) $A'000
1.8	Net operating cash flows (carried forward)	**(116)**	**(382)**
	Cash flows related to investing activities		
1.9	Payment for acquisition of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual property	-	-
	(d) physical non-current assets	-	(5)
	(e) other non-current assets	-	-
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual property	-	-
	(d) physical non-current assets	-	-
	(e) other non-current assets	-	-
1.11	Loans to other entities	-	-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)	-	-
	Net investing cash flows	**-**	**(5)**
1.14	**Total operating and investing cash flows**	**(116)**	**(387)**
	Cash flows related to financing activities		
1.15	Proceeds from issues of shares, options (net of capital raising costs)	30	1,391
1.16	Proceeds from sale of forfeited shares	-	-
1.17	Proceeds from borrowings	-	30
1.18	Repayment of borrowings		(30)
1.19	Dividends paid	-	-
1.20	Other	-	11
	Net financing cash flows	**30**	**1,402**
	Net increase (decrease) in cash held	(86)	1,015
1.21	Cash at beginning of quarter/year to date	1,214	113
1.22	Exchange rate adjustments to item 1.20	-	-
1.23	**Cash at end of quarter**	**1,128**	**1,128**

+ See chapter 19 for defined terms.

Payments to directors of the entity and associates of the directors

Payments to related entities of the entity and associates of the related entities

		Current quarter $A'000
1.24	Aggregate amount of payments to the parties included in item 1.2	44
1.25	Aggregate amount of loans from the parties included in item 1.11	-

1.26 Explanation necessary for an understanding of the transactions

1.24 – payments relate to Directors Fees paid during the quarter.

Non-cash financing and investing activities

2.1 Details of financing and investing transactions which have had a material effect on consolidated assets and liabilities but did not involve cash flows

N/A

2.2 Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest

N/A

Financing facilities available

Add notes as necessary for an understanding of the position.

		Amount available $A'000	Amount used $A'000
3.1	Loan facilities	-	-
3.2	Credit standby arrangements	N/A	N/A

+ See chapter 19 for defined terms.

Reconciliation of cash

Reconciliation of cash at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts is as follows.		Current quarter $A'000	Previous quarter $A'000
4.1	Cash on hand and at bank	13	9
4.2	Deposits at call	1,115	1,205
4.3	Bank overdraft	-	-
4.4	Other (provide details)	-	-
	Total: cash at end of quarter (item 1.23)	1,128	1,214

Acquisitions and disposals of business entities

		Acquisitions *(Item 1.9(a))*	Disposals *(Item 1.10(a))*
5.1	Name of entity	Nil	Nil
5.2	Place of incorporation or registration		
5.3	Consideration for acquisition or disposal		
5.4	Total net assets		
5.5	Nature of business		

Compliance statement

1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.

2 This statement does give a true and fair view of the matters disclosed.

Sign here: Date: 31 July 2014

Company Secretary

Print name: Peter Webse

+ See chapter 19 for defined terms.

Notes

1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.

2. The definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report except for any additional disclosure requirements requested by AASB 107 that are not already itemised in this report.

3. **Accounting Standards.** ASX will accept, for example, the use of International Financial Reporting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

+ See chapter 19 for defined terms.