ACRUX LIMITED (ASX: ACR)

SHAREHOLDER UPDATE

DECEMBER 2004 – FEBRUARY 2005

Dear Shareholder, 1 March 2005

The attached update sets out details of another successful quarter for Acrux's business. We are in a position that few in our sector in Australia can match:

- We are closer to having products in billion dollar US markets – our lead product is in the last clinical trial (Phase 3) before submission to the FDA for marketing approval and another product is expected to start Phase 3 in 2005, following successful Phase 2 results. Both Phase 3 programmes are funded by our partner VIVUS.
- We have proved that we can secure commercial partners for our products (Lilly, Vivus, CSL)
- We have multiple products in development, which will provide more out-licensing opportunities – 7 products are in clinical trials and more in formulation development
- We have an easier path to product approval – with fewer and shorter trials required because we use proven drugs
- We have cash reserves of $29 million – sufficient for the business to reach profitability

Despite this strong position, our share price has fallen since listing, in particular during the last two weeks, driven by erratic, low volume retail trading, which we believe is at odds with our business fundamentals.

We thank Shareholders for their patience and support as we work hard to continue on our path to commercial success and to communicate Acrux's value to the market.

Yours sincerely,

Nuno D'Aquino
Chairman

Igor Gonda
Chief Executive Officer

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Acrux is a dynamic Australian specialty pharmaceutical company developing and commercialising a range of patient-preferred healthcare products for global markets.

Highlights

- Achievements during the quarter continue the significant progress and risk reduction since IPO; Aegis analyst valuation rises to $1.36 per share

- Start of final US trial (Phase 3) with Evamist™ (Estradiol MDTS®) by Acrux's partner VIVUS

- Positive results from large Phase 2b trial with Testosterone MDTS® to treat female hypoactive sexual desire disorder

- Successful completion of Phase 1 trial programme with Fentanyl MDTS® for severe pain; distribution rights for Australia and New Zealand granted to CSL Ltd

- Dosing completed in proof of concept Phase 1 clinical trial with Nestorone MDTS® contraceptive spray

- Start of proof of concept Phase 1 clinical trial with Granisetron MDTS® for prevention of nausea associated with chemotherapy

- December 2004 Half-Year Financial Report shows a 40% rise in revenue to $1.8 million; net loss increased to $3.7 million, reflecting the planned higher investment into development and commercialisation; strong cash reserves of $30.7 million at 31 December 2004 following inflow from IPO of $27.8 million

- JF Capital Partners' shareholding rises to 5% in January following purchases of 3.5 million shares since IPO; total institutional shareholdings rise to approximately 26%

Product Development and Commercialisation

Acrux achieved more important milestones in product development and commercialisation during the December 2004 – February 2005 period. Because we use proven drugs and the same technology platform, we are able to develop multiple products simultaneously at a relatively low cost. Our key task is to show in human clinical trials that we obtain drug levels in the blood that are known to be safe and effective ("pharmacokinetics"). This avoids for many of our products the lengthy and expensive trials typical in the development of new drugs.

Evamist™ (Estradiol MDTS®) for the treatment of symptoms of menopause

In December 2004, VIVUS announced the start of the final clinical trial (Phase 3) in the USA with Evamist™ (Estradiol MDTS®) to treat symptoms of menopause. VIVUS secured a "Special Protocol Assessment" from the FDA, to confirm that this clinical trial could provide the basis for a New Drug Application (NDA), which VIVUS expect to file in 2006. If Evamist™ was approved on a typical timescale this would mean approval to market in 2007. The product is being manufactured by a commercial contract manufacturer in the USA, demonstrating that existing contract manufacturing facilities can be used for our products.

VIVUS will fund all remaining development and manufacturing expenditure for the USA under our Development and Commercialisation Agreement for the USA. VIVUS is due to pay a licence fee of US$1 million to Acrux on or before 29 June 2005 and on VIVUS' achievement of further milestones, Acrux will receive up to US$4 million and also royalties on sales of the product. Acrux retains the rights for the rest of the world and we will look for marketing partners as the US product development progresses.

Testosterone MDTS® for the treatment of HSDD (female hypoactive sexual desire disorder - low libido)

In February 2005, we announced positive results from our Phase 2b clinical trial, in which 261 Australian women between the ages 35-45 participated. These women had low blood levels of testosterone were troubled by low libido. The trial looked at three different doses of testosterone and for the most effective dose, at week 16 a statistically significant increase in the number of satisfactory sexual events was seen, and the number more than doubled compared with the baseline.

VIVUS and Acrux are currently in discussions with the FDA to agree the design of the US Phase 3 trials required for marketing approval in USA.

Our trial results mean that further milestone payments of US$375,000 are due from VIVUS under our Development & Commercialisation Agreement for the USA. On VIVUS' achievement of future milestones, we will also receive further payments of up to US$5.5 million, plus royalties on sales of the product. VIVUS will fund all future development and manufacturing expenditure for the USA. They recently announced an underwritten capital raising of approximately US$30 million, led by a major US broking firm, S.G. Cowen, boosting their funds available for Phase 3 trials. In the meantime we are actively seeking commercial partners for other territories, including Europe. We already have CSL as our partner for Australia and New Zealand.

Procter & Gamble are ahead of us in development of their testosterone patch "Intrinsa". However, in December, an FDA Advisory Committee recommended against approval of their NDA, suggesting that longer safety trials should be undertaken. Whilst this requirement will impact VIVUS as well, it should reduce the time gap between launch by P&G and launch of our product, since VIVUS had not started Phase 3 trials and can now adapt the design accordingly.

Fentanyl MDTS® for the treatment of severe chronic pain

In January 2005, we successfully completed our Phase 1 clinical trial programme with Fentanyl MDTS®. Therapeutic levels of fentanyl were achieved with three different dosing intervals, suggesting that our product can provide effective treatment with greater flexibility than existing products. The strength of the results mean that we do not need to proceed with an additional planned trial, saving $0.5 million. The next step will be a meeting with the FDA to obtain guidance on their requirements for the remaining trials. As fentanyl has been in use for the treatment of severe pain both in cancer patients and other types of chronic pain for a number of decades and sales of a transdermal fentanyl patch are already over US$1. 6 billion per annum, we expect the regulatory requirements to be substantially lower than for a new drug.

On 30 November, we announced another agreement with CSL Ltd to distribute this product in Australia and New Zealand. Acrux retains rights for the rest of the world and will seek commercial partners, particularly for USA and Europe, using information from the FDA meeting.

Testosterone MD-Lotion™ for the treatment of testosterone deficiency in men

In our last Shareholder Update we reported that we had met with FDA following the successful completion of our proof of concept Phase 1 trial. We are now ready to proceed with the remaining development, following FDA's guidance. Because transdermal testosterone for males is already a well established market in USA, the required trials are low risk and moderate cost. Therefore, as indicated in the IPO prospectus, we intend to fund those trials ourselves before we license the product to a commercial partner. This should enable us to secure a larger share of the value of the product in a licensing deal. The first two of the remaining trials will start in March 2005.

Granisetron MDTS® for the prevention of nausea

Today we announced in a media release that dosing has started in a proof of concept Phase 1 trial of our transdermal spray for prevention of nausea, a common side effect associated with chemotherapy. Our aim is to eliminate the need for injections or tablets, helping to minimise distress for cancer patients. The trial will compare the absorption of the drug from our spray with the absorption of the drug from an approved tablet.

Other activity during the period included the establishment of a research partnership with the prestigious University of London School of Pharmacy (ULSOP). Under the agreement, Acrux will sponsor a postgraduate student to conduct targeted, innovative research into transdermal drug delivery. All rights to intellectual property generated as part of this research partnership will be held by Acrux.

Our human pharmaceutical development pipeline and current clinical trials are summarised in tables on the following pages:

Therapeutic Area	World Market US$ Billion P.A.	Product	Clinical and Regulatory Status	Development milestones expected before 30 June 2005
Menopausal symptoms	1.2[1]	Evamist™ (Estradiol MDTS®)	US phase 3 trial started (US IND)	Trial ongoing
Female Hypoactive Sexual Desire Disorder	>1.0[2]	Testosterone MDTS®	Phase 2b trial completed (US IND), with positive results	Discussions with FDA to agree design of US Phase 3 trial programme
Severe pain	5.6[1]	Fentanyl MDTS®	Multiple dose phase 1 trial completed, with positive results	Pre-IND meeting with FDA for guidance on remaining requirements
Anxiety-related	Undisclosed	Buspirone MDTS®	Completed proof of concept phase 1 trial and seeking licensing partners	Remaining development to be agreed with and funded by licensing partners
Male testosterone deficiency	0.4[1]	Testosterone MD-Lotion™	Completed proof of concept phase 1 trial, pre-IND meeting with FDA held	Start next trials in accordance with FDA advice
Nausea	1.3[1]	Granisetron MDTS®	Proof of concept phase 1 trial started	Complete trial
Contraception	4.4[1]	Nestorone MDTS®	Proof of concept phase 1 trial started	Complete trial
Incontinence	1.0[1]	Oxybutynin MDTS®	In formulation development	Continue formulation development
Smoking cessation	0.7[1]	Nicotine MDTS®	In formulation development	Continue formulation development
Niche market products	Undisclosed	Undisclosed	In formulation development	Continue formulation development

[1] Estimated by IMS Health, Inc for 12 months ended February 2004 (IMS Health, Inc., Therapy Area Sales Reports, 2004. Copyright 2004. All rights reserved). [2] No products are currently approved for this market. Based on US female population statistics and assumptions regarding the incidents of the condition, the proportion of subjects seeking treatment and the price of treatment, Acrux estimates that by 2008 the total US market will be in excess of US$1 billion.

Current clinical trials:

Trial Title/Description	No. of Subjects	Current status and next steps
A double blind randomised placebo controlled multi centre study to evaluate the safety and efficacy of once-daily use of Evamist™ spray on moderate-to-severe vasomotor symptoms (hot flushes) associated with menopause. (Phase 3 under US IND)	Up to 500	FDA granted VIVUS Special Protocol Assessment approval. Study started in December 2004. Recruitment of subjects underway
A double blind randomised placebo controlled study to evaluate the effects of different doses of testosterone from Testosterone MDTS® on sexual function in premenopausal women with low libido. (Phase 2b under a US IND)	261	Study completed and positive data reported; full results to be presented at scientific conference
A randomised, three-way crossover evaluation of the steady-state pharmacokinetics of fentanyl following multiple dose administration of Fentanyl MDTS® or a Durogesic® 25 patch. (Phase 1)	12	Study completed successfully. Pre-IND meeting with FDA to be held before June 2005 to discuss remaining development required for approval in USA
A randomised, two-way crossover study to compare the pharmacokinetics of testosterone following application of Testosterone MD-Lotion™ or AndroGel® in men with low serum testosterone. (Phase 1)	6	Study completed successfully. Pre-IND meeting with FDA held to discuss remaining development required for approval in USA. Next studies to start in March 2005.
A study of the pharmacokinetics of Nestorone® after application of Nestorone MDTS® in Postmenopausal Women. (Phase 1)	8	Dosing completed; data analysis expected in the second quarter of 2005.
A study of pharmacokinetics of Granisetron MDTS® for treatment of nausea associated with chemotherapy. (Phase 1)	6	Dosing started; data analysis expected in the second quarter of 2005.

Investor Relations

In January 2005, JP Morgan Chase & Co affiliate, JF Capital Partners Limited, became a substantial holder, as purchases of 3.5 million shares since the IPO took their holding to 5%. In the early part of the quarter, regular institutional buying raised total institutional holdings to approximately 26%.

Share trading since Christmas has been extremely disappointing, with erratic, low value retail trades driving the share price down, despite the announcement of the start of the Phase 3 clinical trial of Evamist™, positive results in the large Testosterone MDTS® 2b trial and successful completion of the Fentanyl MDTS® Phase 1 programme. These are very significant milestones in the development of the Acrux's lead products. The Testosterone MDTS® results generated extensive local and international media coverage, including television, radio and newsprint.

Aegis analyst John Kessell increased his valuation of Acrux to $1.36 per share on a fully diluted basis following our half yearly results, emphasising in his report the reduction in the business risk profile. Aegis is engaged by Goldman Sachs JBWere to provide specialist analysis on Acrux. Wilson HTM analyst Graeme Wald continues coverage and "Bioshares" includes Acrux in its model portfolio.

Chairman Nuno D'Aquino, CEO Igor Gonda and CFO Jon Pilcher will meet with institutions, brokers and analysts in early March to discuss the substantial progress in our commercialisation and development plan since the IPO.

We would like to encourage Shareholders to register for "e-mail alert" in the investor section of our website (www.acrux.com.au), as this is the quickest and most efficient way to receive Acrux news.

Finance

Highlights of our Financial Report for the half-year ended 31 December 2004 were as follows:

- A 40% rise in revenue to $1.8 million, up from $1.3 million, driven mainly by the first revenue from Acrux's grant under the Pharmaceutical Partnerships Program (P3). Revenue included US$625,000 in milestone payments from VIVUS Inc.
- Operating costs increased from $3.5 million to $5.5 million, mainly in staff and external development expenditure, reflecting higher investment into development and commercialisation of Acrux's product pipeline.
- Net loss increased from $2.2 million to $3.7 million
- Net cash inflow from IPO of $27.8 million, resulting in strong cash reserves of $30.7 million at 31 December 2004.

A summary table of our financial results is provided below. For full financial results, please refer to our website to view the Financial Report for the Half-Year ended 31 December 2004.

Summary of financial results ($ million)

6 months ended 31 December	2004	2003
Licensing and R&D revenues	0.9	1.1
P3 grant	0.4	0.0
Interest and other income	0.5	0.2
Total revenue	**1.8**	**1.3**
Total expenditure	**(5.5)**	**(3.5)**
Net loss	**(3.7)**	**(2.2)**
Other cash flows	0.0	(0.1)
Net cash outflow before new capital	**(3.7)**	**(2.3)**
New share capital net proceeds	**27.8**	**0.2**
Net cash inflow/(outflow)	**24.1**	**(2.1)**
Net cash	**30.7**	**8.8**

Our target remains sustainable profitability in the financial year ending 30 June 2008. We will prudently manage our cash reserves over the period to 30 June 2007, aiming to always have a comfortable buffer. We currently have three significant sources of revenue; our licences to VIVUS of Evamist™ and Testosterone MDTS® for the USA, our global licence to Eli Lilly of veterinary products and our P3 grant. Our development efforts are providing more products that can be licensed to add new revenue streams.

As previously signalled and as indicated by the half-year results, in the short term we have deliberately increased our development expenditure by more than our revenue increase, in order to get products to revenue earning as quickly as possible to exploit our intellectual property fully. This means that our loss for the year ended 30 June 2005 will be higher than in the previous year. The resulting revenue growth will enable us to progress towards our profitability target.

Intellectual Property

Acrux's patent portfolio, summarised in the table below, continues to expand, with 4 patent families entering into 14 different countries[†], 6 patent families filed as a single Patent Cooperation Treaty (PCT) international application (all 124 member countries are automatically designated) and 2 new provisional patent applications filed.

		Family member	USA	Europe	Australia	ROW
Patent Family 1	Enhancer Patent	a	G	P	G	P/G
	Enhancer Patent	b	G	n/a	n/a	n/a
	Enhancer Patent	c	P	n/a	n/a	n/a
	Enhancer Patent	d	P	n/a	n/a	n/a
	Enhancer Patent	e	P	n/a	n/a	n/a
	Enhancer Patent	f	P	n/a	n/a	n/a
	Enhancer Patent	g	P	n/a	n/a	n/a
	Enhancer Patent	h	P	n/a	n/a	n/a
	Enhancer Patent	i	P	n/a	n/a	n/a
	Enhancer Patent	j	P	n/a	n/a	n/a
	Enhancer Patent	k	P	n/a	n/a	n/a
Patent Family 2	Dispensing Device	a	P	P	P	P
		b	n/a	n/a	n/a	P
Patent Family 3	Delivery Patent		P	n/a	n/a	P
Patent Family 4	Delivery Patent		P	P	P	P
Patent Family 5	Delivery Patent		P	P	P	P
Patent Family 6	Delivery Patent		P	P	P	P
Patent Family 7	Delivery Patent		P	P	P	P
Patent Family 8	Dispensing Device		PCT	PCT	PCT	PCT
Patent Family 9	Dispensing Device		PCT	PCT	PCT	PCT
Patent Family 10	Delivery Patent		PCT	PCT	PCT	PCT
Patent Family 11	Delivery Patent		PCT	PCT	PCT	PCT
Patent Family 12	Method and Device		PCT	PCT	PCT	PCT
Patent Family 13	Delivery Patent		PCT	PCT	PCT	PCT
Patent Family 14	Dispensing Device		-	-	Prov	-
Patent Family 15	Delivery Patent		-	-	Prov	-
Patent Family 16	Dispensing Device		-	-	Prov	-
Patent Family 17	Dispensing Device		-	-	Prov	-
Patent Family 18	Delivery Patent		-	-	Prov	-
Patent Family 19	Delivery Patent		-	-	Prov	-
Design Family 1	Dispensing Device		G	G	G	G

G = granted; P = pending; Prov = provisional; PCT = Patent Cooperation Treaty; ROW = rest of World; [†]Europe = 1 country

Publications and Presentations

Acrux delivered two presentations at the Australian Pharmaceutical Science Association (APSA) annual conference held in Melbourne on 5 December 2004:

- "Prevention of undesired effect or overdose with transdermal fentanyl"; and
- "Less is More: Non-occlusive systems for Transdermal delivery"

CEO & Managing Director, Igor Gonda has been invited to present at the Australian Biotechnology Summit 2005 in Sydney in July. The theme for the Summit is 'Commercialisation and partnership with big pharma: What are the opportunities?'.

Personnel

Two senior appointments have been made as we expand our commercial activities.

- Peter Willcocks as General Counsel & Company Secretary; and
- Professor Richard Guy to the Scientific Advisory Board

Peter comes with over 25 years experience in commercial and corporate law. Prior to joining the company he was a partner with Landers & Rogers, Lawyers, with his principal areas of practice being international pharmaceutical commercial contracts, takeovers, mergers & acquisitions, Corporations law, corporate governance and general commercial agreements. His experience will be invaluable as we embark on negotiating further commercial deals for our products.

Peter will be appointed Company Secretary by the Board in due course; in the meantime, Jon Pilcher continues as Company Secretary as well as CFO. Peter's appointment will enable Jon to focus fully on finance and investor relations.

Richard is Professor of Pharmaceutical Sciences at the University of Bath, UK, with a long standing record of valuable contributions to both industry and academia. He is recognised as one of the world leaders in transdermal drug delivery and received an M.A in Chemistry from Oxford University and his Ph.D in Pharmaceutical Chemistry from the University of London. Professor Guy has authored more than 200 peer-reviewed articles, 70 book chapters, and co-edited 7 books. Professor Guy joins the other global scientific leaders who help Acrux with strategic decisions on the development of our technologies and patient-preferred products for global pharmaceutical markets.

About Acrux

About Acrux (ASX: ACR)

- Acrux is a specialty pharmaceutical company, developing and commercialising a range of patented, patient-preferred healthcare products for global markets, using its innovative technology to administer drugs through the skin.

- Acrux's product pipeline includes treatments of hormonal deficiencies, pain, central nervous system disorders and urinary incontinence, as well as a contraceptive.

- 16 human clinical trials have been completed with 6 different drugs and the lead product, Evamist™ (Estradiol MDTS®), is currently in a phase 3 clinical trial in the USA.

- Acrux has licensed USA rights for Evamist™ (Estradiol MDTS®) and Testosterone MDTS® to **VIVUS** and AUS/NZ distribution rights for Testosterone MDTS® and Fentanyl MDTS® to **CSL Limited**. Acrux has also licensed its technology to **Eli Lilly** for veterinary healthcare products, and to **Connetics** for anti-psoriatics and local anaesthetics.