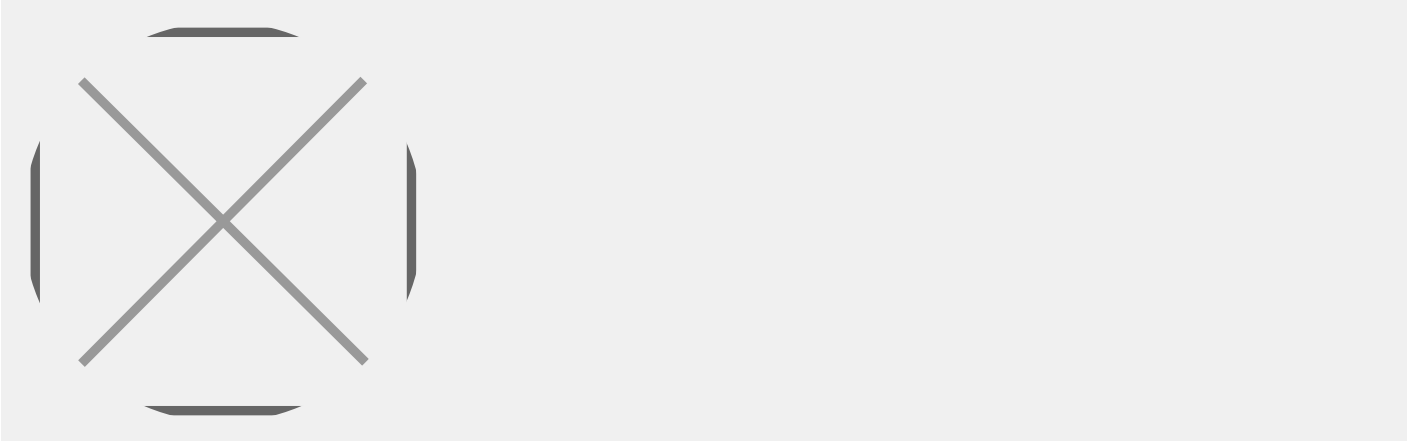
Interview with Andrew Giddy, CEO, Nucleus Network



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Tags: Nucleus Network

Please introduce Nucleus Network and the role it plays in the Australian pharmaceutical sector.

Nucleus Network is an early-phase clinical research business, and is somewhat unique, as it is a not for profit organization, being wholly-owned by the Baker IDI Heart and Diabetes research institute. Originally, Nucleus Network was set up with a grant from the Victorian government, but since then, it has established a commercially based business doing early phase clinical trials. Nucleus Network has a 30-bed in-patient clinical trials unit adjacent to the Alfred Hospital, which is the major tertiary teaching hospital in Melbourne, and performs about 30 to 40 phase I clinical trials each year in that unit with a mix between healthy volunteer and patient studies. The organization does the standard phase I studies, although in recent years, there has been a higher percentage of first in man studies including first in man biologic studies. For the healthy volunteer studies, Nucleus Network has its own medical director and staff. The Medical Director is a professor of clinical pharmacology, and is the principal investigator on the healthy studies. For the patient studies, the principal investigator(s) are from the Alfred hospital, so the organization will work with the relevant group, whether in oncology, rheumatology, gastroenterology, etc., and the relevant expert principal investigator to conduct all the operational aspects of the study. Nucleus Network is unique in being very closely linked to a tertiary teaching hospital, with access to the specialist principal investigators for early phase studies, and also in the same building as a large number of research institutes. As a result of this access to basic research institutes, Nucleus Network is able to undertake more proof of principle in phase I studies, with more esoteric biomarkers being built in to get an early signal of efficacy, even in a traditional safety / dose finding type phase I study. A linkage and co-location with the research institutes allows Nucleus Network to do close to source biomarker assays- which may include cytokine stimulation assays, or FACS analysis. Nucleus

Network mostly uses many of the co-located research institutes to undertake these assays and their linkage with the Baker Heart Institute also allows access to many experimental pharmacology-type studies, isolating individual vessels in an in vivo setting but ex vivo, so there are many special techniques that can be brought into play. Nucleus Network looks at all therapeutic areas, and makes use of the myriad of expert opinion nearby. The organization basically came to full capacity at the Alfred Hospital at the end of 2006, so since this time we have built a second unit at the Austin hospital, which is another tertiary teaching hospital, linked to Melbourne University's Medical School. With the Alfred Hospital linked to Monash University Medical School, Nucleus Network is associated with the two major teaching medical schools in Melbourne. Early phase trials makes up 90% of Nucleus Network's business, but we also operate in two other areas, the first of which is called Clinical Trials Consulting, where there is a consultancy group geared toward the local biotech market, to help them go from preclinical studies into the clinic for the first time. Nucleus Network starts working with these companies a year before they are ready to move to the clinic, and helps them do a preclinical gap analysis, to determine whether they have all the data needed to start their clinical trials, and possibly to write their first drug brochure, to fill in all the gaps. This is especially necessary for the smaller biotechs, because in the beginning they may count between 1-10 people, so they really don't have the clinical skills. Nucleus Network therefore helps generating a clinical development plan, and to seek out grant funding from sources like Commercial Ready, when the program still existed. About 80%-90% of Nucleus Network's work is for big pharma and biotech companies, working with eight of the top 10 pharmas, and three of the top five biotechs on a global basis. That makes up most of Nucleus Network's work, which means most of our efforts are toward export services, with local biotechs comprising five or six studies per year. The third area of business is Nucleus Network education, which involves teaching Good Clinical Practice (GCP) based on the American Association of Clinical Research Professionals (ACRP) course, in addition to facilitating the GCP certification examination, which are the global exams run three times yearly. Nucleus Network puts its entire staff through that program, and has trained over 900 research staff, mostly clinical research coordinators and investigators. Nucleus Network also identified a gap in the market, in public hospitals doing investigator-initiated studies, which is separate from the industry CRA area. In training this segment, for us, it's really about building the industry, and is not a profitable part of the business per se. As a not for profit, our profit goes to the subsidization of those programs, because price-wise it's hard for research nurses in hospitals to afford taking a GCP course.

This last example illustrates one aspect of operating as a not-for-profit, but what other differences would you point to in running Nucleus Network under this structure?

Part of the advantage of being a not-for-profit is that it allows flexibility in terms of reinvesting in infrastructure and equipment. As a relatively new player in the market, Nucleus Network follows a strategy that is very much quality-focused, and sees itself as having to be at the highest level as a

niche provider. Because there are so many phase I units around the world, Nucleus Network couldn't just be a basic bioequivalence unit because we haven't 300 or 400 beds. Australia is not a low-wage country in terms of staff and so on, so the research has to be at the sharp end in terms of executing the early phase studies that big pharma companies care the most about in terms of risk, which is why Nucleus Network is seeing a lot of first in man and biomarker studies. The appeal of Nucleus Network compared to some of the other units is that we're small, and doing one or two studies concurrently, and can give our clients full attention. This compares favourably to a 400 bed scenario, where clients tend to get lost in the system. Nucleus Network invests in the latest ECG and telemetry equipment, in order to provide world class standards and offerings attractive to big pharma. The organization is also audited by the FDA and NIH, which are international standards to be met in an international market; as such it's not really about domestic competition. There're only four specialist phase I facilities spread out in Australia's capital cities, and although there's a little bit of competition between us, it's more about competing against the 8,000 beds in North America, than about the 150 beds in Australia.

What is the pitch to those American companies, for instance, to go beyond those 8,000 beds that are so much closer? What is the biggest value added for Australia and Nucleus Network?

A lot of big pharma and biotech companies like Australia because studies can be done before filing an IND, to get patient data before going to the FDA. If companies have no data when first approaching the FDA, they may have to follow FDA advice on their development plans, but if they go with some initial safety and pharmacokinetic data, they can cut a significant amount of required time away, as opposed to relying on two dog and a rat study, for example. This gives the companies more flexibility to engage with the FDA on the clinical components. It seems contrary, but Nucleus Network sees local biotechs in Australia going to the US and filing an IND before they've started, to try and get a tick in the box from the FDA to help with fundraising, whereas the North American companies tend to come to Australia before they've filed an IND, to get some data and reduce the size and accelerate their program. A further advantage for Nucleus Network is having the niche provider status and being responsive and relatively quick. Australia's regulatory system is favourable, not having to go through the whole IND application and maintenance process. All phase I studies can be addressed by the local ethics committee, so as long as there is a competent ethics committee with the right scientific subcommittee, they can do the full evaluation to avoid going through a central regulatory process. Instead, it's a devolved regulatory process, of generally four to six weeks, after which point, a company can start immediately. Start-up times are also quick, and what's really important is measuring the time from first protocol to first patient in. North America has fast ethics turnaround times, but using this measure, the timeline in Australia is more than competitive. Overall, Nucleus Network operating in Australia with a strong regulatory system, the pre-IND studies, access to specialist research centres which is helpful in proof of

principle and biomarker work, having specialist principal investigators, having the unit co-located in a teaching hospital, are all strategies Nucleus Network has followed to its competitive advantage.

Given that Nucleus Network is fairly new, yet already has partnerships with eight of the 10 big pharma and three of the five big biotech, was it from their side in recognizing the organization's potential, or from your end?

Nucleus Network is not-for-profit, but that doesn't mean we're not commercially oriented. We work hard to chase down leads, and our business development staff will be in North America between two and four times per year, and we have a full-time marketing manager based in San Francisco covering the Bay area. The key with large pharmas and biotechs is that they do have large volumes of studies, so it's all about track record. If you can get them through the door and get a first study under the belt and do it well, then you get the second, third, fourth, etc. Nucleus Network finds it builds up momentum with each of them, and this keeps things busy. One of the issues for the organization during this year has been the fluctuation in the Australian Dollar, which at the beginning of 2008 was at $0.82 USD, before reaching heights of $0.98 USD and falling back down to $0.83 USD. Certainly, Australia was price competitive relative to the US and Europe. It lost some of that price competitiveness during part of this year, but since the AUD has fallen back down again, it is now again very attractive to the USA, which is good. Australia has always stayed relatively price competitive with Europe because it seems to be more expensive, particularly in terms of time costs because of the whole European clinical trials directive issue. Nucleus Network does quite a lot of European big pharma work, but not a lot of European biotech work. There's not a lot that gets out of Europe, and that's the frontier all the Australian units have identified that none is tapping into. There's a group formed called Early Phase Clinical Research Australia, which is the association of the four commercially operating or specialist phase I units. The group is looking at the synergies between us, in developing a multi-site phase I offer, that would really be about when you need to go to multiple phase I sites to capture particular patient populations. We can offer cities with 12 million people amongst the four units in total, creating a very competitive recruitment pool. The Australian regulator, the TGA, does not have any audit capability, unlike the FDA, although there are plans to change this year, which would be a good thing for local industry. One of the things Nucleus Network is doing in the early phase group is implementing its own accreditation scheme based on the MHRA accreditation for the phase I units, following the TeGenero issues in 2006. This is yet another way to be internationally competitive, even if the regulator doesn't require such measures.

Are there any internationally competitive examples you would like to showcase as case studies to demonstrate what Nucleus Network can do?

One example that shows the organization's flexibility occurred when a North American biotech firm was developing a new combination of an inhalation agent. To make that product, they would have

to produce it to a GMP standard out of a GMP-licensed facility. In Australia, we were able to manufacture in-house to a GMP standard but not in a GMP-licensed facility, which is possible under Australian regulations. As a result, the company told us we had shaved twelve months off their development plan.Since that, we've heard from three mid-sized biotechs who heard that story from the company directly. There's a strong word of mouth regarding Nucleus Network's flexible attitude about what can be done, and not staying too rigid in terms of what's possible.

What is the role of, and what have you heard in terms of feedback from, your San Francisco-based marketing manager?

She's been working on creating awareness of Australia as a destination, because the US tends to start inward looking, until they step outside, at which point they become very relaxed about working internationally. She has done things like run Australian drug development seminars in the Bay Area, where we bring in people and tell them about how Nucleus Network works and what can be done in Australia, in terms of thinking outside conventional areas of operation, and knowing what the market wants. When our business development staff travel to the US, she will set up meetings, and on our last trip in the week pre-BIO, we saw 20 companies, and five studies came out of five days of work. The final formulation step for the investigational product is an important one that takes time as well, and if you can do the final encapsulation of the product on-site, as opposed to running it through a facility and waiting, that's quite a big issue. Nucleus Network has just invested in another business to have a GMP-licensed facility with four clean rooms to be able to do more just-in-time formulation and manufacture. In terms of niche offers, Australia is a good place to do some ethnopharmacology studies, such as Japanese bridging, which was traditionally done in Hawaii. However, the requirement from the Japanese regulator is such that much of that population no longer qualifies. Last year, Nucleus Network performed three Japanese-Caucasian metabolism studies, and there is a full-time Japanese doctor on staff to do those studies. That's an area that will keep growing, and Nucleus Network is just now setting up for a Japanese-Caucasian-Chinese study, and is hoping to do more to serve the Chinese and Korean markets.

Over the next five to 10 years, where do you want to bring Nucleus Network?

Nucleus Network will stay in the niche provision area, and as phase I studies continue to increase in complexity, our challenge will be to keep meeting those complexity hurdles, which I think we will be able to do, because the basic science research base in Australia is so strong. If we stick with the strategy of staying close to research institutes, Nucleus Network will have access to the cutting edge science and we can translate that into practical uses. Ideally, Nucleus Network can replicate this model in the cities where there are major research institutes, and will probably get to a point where this will be the case, whether in direct investments or through partnerships. The first challenge will be to access patient pools, perhaps partnering with developing nations like India or China, to reach untreated disease populations. Although Nucleus Network tends to operate around

early phase work, for local biotechs we have helped from pre-clinical into clinic, and we will also help into phase 2 and 3, because it’s always nice to see things develop locally.

What is your final message to Pharmaceutical Executive readers?

Nucleus Network provides access to cutting edge technology, whether that’s infrastructure within facilities, or expertise of principal investigators. There’s nimbleness around what we can do, and the organization can always adapt to the circumstances to get the job done.

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