

## NIH Program to Study Patients with Mystery Diseases

For thousands of frustrated patients with diseases that cannot be explained or diagnosed—even by leading specialists in their field—enrollment in clinical trials has not been an option. Without a definitive diagnosis, they are ineligible to participate.

Now, through a pioneering program launched by the National Institutes of Health (NIH), there may be hope. The new trans-NIH initiative, called the Undiagnosed Disease Program, will concentrate its research efforts on patients who suffer from unknown, thus unstudied, illnesses.

The program will be headed by William Gahl, M.D., Ph.D., clinical director at the National Human Genome Research Institute

(NHGRI). Both John Gallin, M.D., director of the NIH Clinical Center; and Stephen Groft, Pharm.D., director of the NIH Office of Rare Diseases will also be directly involved in its operation.

The key to the project is its collaborative nature, using the skills of more than 25 NIH investigators with expertise in endocrinology, immunology, oncology, dermatology, dentistry, cardiology and genetics.

The initial pilot study will choose 50 to 100 subjects per year, referred to the program by physicians across the U.S. The first patients will enter the program in July 2008.

The NIH Clinical Center is the largest med-

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## CDER's Woodcock Details Expanded Authority, Sentinel Concept at Post-Approval Summit

Opening the Post-Approval Summit at Harvard, keynote speaker Janet Woodcock, M.D., director of the Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA), outlined her agency's expanded authorities in the area of post-approval research oversight brought about by the passage of the FDA Amendments Act (FDAAA) into law at the end of March.

"FDAAA stipulates many new tasks and authorities for CDER," said Woodcock.

Among its new authorities, CDER will be able to require a Risk Evaluation and Mitigation Strategy (REMS), which is a

strategy to manage a known or potential serious risk associated with a drug or biological product. A REMS will be required if FDA finds that a REMS is necessary to ensure that the benefits of the drug or biological product outweigh the risks of the product, and FDA notifies the sponsor. A REMS can include a Medication Guide, Patient Package Insert, a communication plan, elements to assure safe use, and an implementation system, and must include a timetable for assessment of the REMS. Some drug and biological products that previously were approved/licensed with risk minimization action plans (RiskMAPs) will now

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**Industry Briefs****CROs**

■ Houston, Texas-based CRO **Pharm-Olam International**, along with its sister-company **MB Quest**, opened a new office in St. Petersburg, Russia. The office is Pharm-Olam's third location in the country to date, after expanding into Moscow and Novosibirsk. The new office is set to house 20 clinical staff by the fourth quarter of 2008. The company stated it has been conducting studies in Russia since 1997, but was using regional employees to monitor trials in St. Petersburg. "Because of the concentration of state-approved sites for research and the continued interest from sponsors, it made sense to establish a permanent office there," said Eugene Barg, president of MBQ. Like Pharm-Olam, MB Quest is a subsidiary of the POI Group. It operates in Russia, Ukraine, Georgia, and Belarus. It is also a founding member of the Association of Clinical Trial Organizations in Russia (ACTO). Pharm-Olam International Group now has 25 offices worldwide.

**Technology**

■ UK-based eClinical company **ClinPhone** established a new office in Paris to further service its existing clients in the country and expand its presence in the European region. The office will be headed by Damien Tremolet who serves as director of opera-

tions for the company. ClinPhone stated that having a local presence increases its ability to maintain face-to-face relations, on-site trial consulting and help clients with language obstacles. Jacques Rudelle, associate director of business development, will assist in its operations. ClinPhone announced it inked a major contract with Veeda Oncology, a new specialty subsidiary of Veeda Clinical Research for the use of ClinPhone's clinical trial management system, TrialWorks. TrialWorks provides access to real-time trial data and detailed reports. Veeda Oncology will be using the system at large sites in India, France, Germany and the U.S. ClinPhone stated it was ultimately TrialWork's user interface and monitoring module that led to winning the contract. The module allows its client's monitors to upload data remotely and produce necessary reports in Microsoft Word format.

■ Ft. Lauderdale, Fla.-based eClinical firm **Omnicom Systems** landed a five-year, multimillion dollar enterprise agreement with a "major West Coast biotechnology company" for the use of its electronic data capture (EDC) product, TrialMaster. The agreement calls for its use in up to 10 trials per year. The deal includes licensing, services and tech support.

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**Features** (continued from page 1)

**NIH**

ical center in the world dedicated exclusively to clinical research. Each year, about 10,000 patients—half with rare conditions—are admitted, many of these are selected to become subjects in studies.

“Right now, the great majority of the patients come to fit into one of 1,500 protocols. This new venture will include patients who do not clearly fit into any protocol to see, and in some cases, we’ll end up after seeing these patients probably creating new protocols that don’t exist,” said John Gallin, director of the NIH Clinical Center during the

media briefing announcing the program.

The aim of the program is not only to focus on helping sick patients whose illnesses have been left out of clinical research. Through the study of these patients, researchers will gain knowledge that can advance the effort to combat known diseases as well.

“The history of biomedical research has taught us that careful study of baffling cases can provide new insights into the mechanisms of disease—both rare and common,” said NIH director Elias Zerhouni, M.D.

The NIH Office of Rare Diseases has contributed an initial annual funding grant of

\$280,000 and the program will be looking to patient advocacy groups for further financing.

Gallin explained that because this was an “intramural program,” the project would be able to take advantage of the more than \$900 million in existing clinical resources.

“I think it’s important to understand too that we’re receiving services both from... the National Human Genome Research Institute, and all the other institutes that are providing services or personnel and the intellectual power that comes with it. We’re the beneficiaries of an unbelievable system here at the NIH,” added Stephen Groft.

**Woodcock**

be deemed to have REMS.

At the end of Woodcock’s talk and others’, audience members from pharma and CROs asked what the difference between a REMS and a RiskMAP was and whether the REMS would replace the RiskMAP. These questioners were invariably referred to the agency’s lawyers. REMS relationship to RiskMAPs was not made clear at the conference.

Woodcock discussed plans for the agency’s pharmacovigilance and active surveillance. The goals for the agency’s new system are to include 25 million patients by July 1, 2010, and 100 million patients by July 1, 2012. “It’s no problem to set up the system, analyzing data is the problem,” said Woodcock. But she did also express budgetary concerns.

Woodcock then described a brand-new concept that is being introduced at the agency, the “Sentinel Concept,” whose purpose is “to ensure drug safety throughout the drug lifecycle by giving equal focus to oversight of drug development and post-marketing safety.”

The Sentinel Concept will use transactional data such as health claims and electronic health records. The agency plans to partner with the data owners to figure out how they can share the information and form a distributed network. “We’ve had tremendous enthusiasm and encouragement from the data owners. There are a tremendous number of pilot projects,” she said. These pilot projects are being sponsored by private parties that are doing research about how best to set up the system as well as evaluating the feasibility and robustness of analyses.

But there are many issues to be ironed out relating to governance, communication, privacy, access to data and healthcare provider burden that CDER will be addressing over the next six to nine months. Woodcock also expressed the need for the “right mix of staff with appropriate skills” and the need to “work in partnership with the healthcare system.”

But Woodcock stressed that the timing was right. “We couldn’t have done this before because we didn’t have the tools.” She expressed the desire to work in partnership with the healthcare system and remove the tension that has existed there.

“What we’re dealing with here is uncertainty, uncertainty, uncertainty... We know whatever decision we make, we will be criticized,” concluded Woodcock.

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## Profile: Predictive Pharmacokinetic Services Company

Simcyp Sheffield, UK

An interview with Steve Toon, Ph.D., executive director

**Year founded:** 2001

**Employees:** 33

**Tel:** +44 (0) 114 292 2322

**Email:** s.toon@simcyp.com

**Web site:** www.simcyp.com

### How and why was Simcyp founded?

Simcyp was a spinout from the Department of Molecular Pharmacology and Therapeutics of the University of Sheffield, UK. The founding scientists, Professor Geoff Tucker and Professor Amin Rostami, have internationally recognized reputations in the field of drug metabolism and molecular pharmacology, and specifically in relating *in vitro* observations of drug metabolism to *in vivo* pharmacokinetics: the area of *in vitro/in vivo* extrapolation. The fundamental basis of Simcyp is the ability to take *in vitro* experimental data that relates to drug metabolism and disposition such as drug disappearance in the presence of drug metabolism enzymes or other *in vitro* systems, such as liver microsomes, and quantitatively take those data through physiologically-based pharmacokinetic models to predict what the observations are going to be *in vivo*.

When Simcyp first started, its predominant focus was on predicting drug clearance (drug elimination). On the back of this, one of the main clinical problems that we were able to set ourselves to was the prediction of drug-drug interactions because most of the important drug-drug interactions involve interaction with drug metabolizing enzymes. And indeed we've now had a lot of success in this area with various publications by Simcyp users that show that, armed with *in vitro* experimental data, they are very good at being able to predict whether there will be significant issues with clinically impor-

tant drug-drug interaction with new drug molecules that are in early development. This ability is having significant impact on the number of drug-drug interaction clinical trials that they need to do. This approach is also enabling them to prioritize their resources so they can say, 'Okay, that drug-drug interaction is potentially so clinically important that we need to look at that in detail in the clinic early on,' or in other instances saying, 'Okay, we may need to look at that in the clinic but we don't need to do it until later on in phase II or phase III. So it helps them manage their resources as well.

### What differentiates Simcyp from other predictive pharmacokinetics services companies?

The Simcyp Simulator can generate virtual clinical populations such as healthy volunteers, geriatric populations, pediatric populations, Japanese populations or populations with certain clinical conditions or diseases. These populations are generated by random statistical sampling from databases that contain information on the physiological mechanisms, and their variability within the human population as a whole, that determine the pharmacokinetic processes of drug absorption, distribution, metabolism and excretion (ADME). Within these virtual populations, using experimentally derived *in vitro* ADME data, physiologically-based pharmacokinetic modeling can be performed to predict the

pharmacokinetics of the drug in the real patient population.

### Tell me about the Simcyp Consortium.

The only companies that access or utilize the Simcyp Simulator product are members of the Simcyp Consortium. To become a license holder of the Simcyp Simulator you join a consortium of companies and regulatory bodies that meet annually to discuss the general scientific issues surrounding *in vitro/in vivo* extrapolation. They debate, discuss and vote upon what problems they would like to see solved in the next version of the Simcyp Simulator. This meeting is held in September, and all the companies get together to discuss the scientific advances in the area of *in vitro/in vivo*, and from a list of probably 20 or 30 items that they see as scientifically relevant they will choose six that they would like to see introduced into the next version of the Simcyp Simulator, which is released annually. This enables Simcyp to continually refine the product in line with the users' wishes. The Simcyp Consortium guides the future development of the Simcyp Simulator. There's a significant training and education component around the area of *in vitro/in vivo* extrapolation provided for consortium members and we conduct various seminars and workshops around the world. This year, we'll have workshops in Switzerland, Boston in June, Sheffield in

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## Profile: Predictive Pharmacokinetic Services Company (continued from page 4)

September and San Francisco in November. Next year, we'll be in Japan. At the moment, there are 18 members of the Simcyp Consortium, which includes 11 of the top 15 pharmaceutical companies, in terms of R&D expenditure. In addition, there are several affiliated drug regulatory bodies, such as FDA, and many affiliated academic institutions. In the coming months we're organizing a training workshop within FDA, in the area of *in vitro/in vivo* extrapolation with a focus on *in silico* prediction of drug-drug interactions.

### Can smaller companies benefit from the Simcyp Simulator?

We are servicing the small biotech or pharmaceutical companies by allowing them access to Simcyp consultancy services. One approach is that people from the pharma company can visit our offices in Sheffield, bring their data and work alongside our scientists in the use of the simulator. Alternatively, they can send us their *in vitro* data, and we can do the analysis for them and generate a report. The real interest from a lot of these smaller companies is that very often their aspiration is to license on their drug. Some of the smaller companies will move into full clinical development, but very often they will develop a lot of the preclinical package and then look for clinical co-development with one of the pharmaceutical majors. Using *in vitro* ADME [absorption, distribution, metabolism and excretion] data with the Simcyp Simulator, these smaller organization can start to generate a 'virtual clinical package' exploring possible issues with drug-drug interactions or pharmacokinetic issues in particular patient or ethnic groups. An added attraction for

these companies adopting this approach is that there is a high likelihood that they will be looking to co-license or co-develop their product with one of the companies that is already a member of the Simcyp Consortium. So, these smaller companies can provide information to organizations that have already bought into the Simcyp philosophy and concept and present them with data that they can understand. So whilst at the moment the members of the consortium are mostly large pharma, we can see that taking advantage of Simcyp consultancy services is something that can be of significant interest to the smaller companies.

### What challenges do you face?

There is still a degree of skepticism within the drug community about the role that modeling and simulation has to play within the drug development process. Drug development historically has been driven almost exclusively by experimentation and there is still a large number of people within the pharmaceutical industry who only believe data that have been gathered experimentally. This works on the assumption that experimental data themselves are completely reliable and error-free. Fundamentally, drug development is a quantitative process, and it is mathematics that threads together the underlying sciences. Out of commercial necessity, industry is now realizing, however, that it cannot afford to fund drug development based on pure empiricism. It's having to look at other ways in which it can maximally use the resources at its disposal.

Additionally, industry is becoming increasingly concerned about being held accountable for clinical

scenarios that they could never have anticipated were going to occur. If they were going to try to explore the entire clinical surface of likely scenarios during clinical trials experimentally, they do not have enough time and they certainly don't have enough money. So, the only way they can really start to assess the boundaries in which their medicine is going to be effective and safe is within the safety of a computer. But at the moment, one of the challenges is getting people to be more comfortable with accepting and relying upon data that are generated within a computer.

### What are Simcyp's plans for growth?

The consortium members pay a membership/licensing fee to access the Simcyp Simulator. One of the consortium members has 14 licenses within their company worldwide and we see increasing uptake of licenses within consortium companies as a major driver to growth. We also see an increasing uptake of interest in Simcyp consultancy services. That is something over the next couple of years that we're putting significant resources in to provide an applied consultancy that can service the smaller pharmaceutical organizations.

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## Drug & Device Pipeline News

Company	Drug/Device	Therapeutic Area	Status	Sponsor Info
Advaxis	Lovaxin C	cervical intraepithelial neoplasia	IND filed with the FDA, phase II trials planned	(732) 545-1590 www.advaxis.com
VGX Pharmaceuticals	VGX-3100	cervical cancer	IND filed with the FDA	(267) 440-4200 www.vgxp.com
VGX Pharmaceuticals	VGX-3400	avian influenza	IND filed with the FDA	(267) 440-4200 www.vgxp.com
BioMarin	PEG-PAL	phenylketonuria	Phase I trials initiated enrolling 35 subjects	(415) 506-6700 www.biomarinpharm.com
KAI Pharmaceuticals	KAI-1678	pain	Phase I trials initiated in Australia	(650) 244-1100 www.kaipharmaceuticals.com
Lpath	ISONEP	age-related macular degeneration	Phase I trials initiated in the US	(858) 678-0800 www.lpath.com
NeoPharm	LE-DT	solid tumors	Phase I trials initiated enrolling 30 subjects in the US	(847) 887-0800 www.neopharm.com
Omeros	OMS201	inflammation during urological surgery	Phase I trials initiated enrolling 24 subjects in the US	(206) 676-5000 www.omeros.com
ImClone Systems	IMC-A12	pancreatic cancer	Phase I/II trials initiated	(212) 645-1405 www.imclone.com
KaloBios	KB001	<i>pseudomonas aeruginosa</i>	Phase I/II trials initiated enrolling 36 subjects in France	(650) 843-1897 www.kalobios.com
Trophos	TRO19622	non alcoholic steato hepatitis	Phase IIa trials initiated enrolling 30 subjects in France	+33 (0)491 828 282 www.trophos.com
Abiogen Pharma	ABIO 08/01	anxiety disorders	Phase II trials initiated in Italy	050 3154101 www.abiogen.com
Alizyme/Prometheus	COLAL-PRED	ulcerative colitis	Phase II trials initiated enrolling 200 subjects in the US	+44(0)1223 896000 www.alizyme.com

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**Drug & Device Pipeline News** (continued from page 6)

Company	Drug/Device	Therapeutic Area	Status	Sponsor Info
Osiris	Prochymal	chronic obstructive pulmonary disease	Phase II trials initiated enrolling 60 subjects	(410) 522-5005 www.osiristx.com
Palatin Technologies	PL-3994	hypertension	Phase II trials initiated enrolling 35 subjects	(609) 495-2200 www.palatin.com
Protox Therapeutics	PRX302	benign prostatic hyperplasia	Phase II trials initiated enrolling 30 subjects	(604) 688-0199 www.protoxtherapeutics.com
Sunesis	voreloxin	acute myeloid leukemia	Phase II trials initiated enrolling 55 subjects in the US	(650) 266-3500 www.sunesis.com
Telik	Telintra	myelodysplastic syndrome	Phase II trials initiated enrolling 86 subjects	(650) 845-7700 www.telik.com
Telik	Telintra	chemotherapy-induced neutropenia	Phase II trials initiated enrolling 135 subjects	(650) 845-7700 www.telik.com
Alba Therapeutics	larazotide acetate	celiac disease	Phase IIb trials initiated enrolling 106 subjects internationally	(410) 319-0780 www.albatherapeutics.com
Ergonex Pharma	Terguride	pulmonary arterial hypertension	Orphan drug designation granted by the FDA	+41 (0) 71 788 4065 www.ergonex.com
Phytopharm	Myogane	amyotrophic lateral sclerosis	Orphan drug designation granted by the EMEA	+44 (0)1480 437697 www.phytopharm.com
InterMune	pirfenidone	idiopathic pulmonary fibrosis	Fast Track status granted by the FDA	(415) 466-2200 www.intermune.com
Salix	balsalazide	ulcerative colitis	FDA approvable letter	(919) 862-1000 www.salix.com
Pharmaxis	Aridol	asthma	Approved in Germany	+61 2 9454 7200 www.pharmaxis.com
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## Trial Results

### Cardiology/ Vascular Disease

■ **Sanofi-Aventis** issued positive results from a phase III trial of **Multaq** for the treatment of atrial fibrillation/arrhythmia. This double-blind, placebo-controlled, randomized study, dubbed ATHENA, enrolled 4,628 subjects across several international sites. The subjects received Multaq 400 mg twice daily or placebo with a maximum follow-up of 30 months. The results showed that treatment with Multaq significantly decreased the risk of cardiovascular hospitalizations or death from any cause by 24% ( $p=0.00000002$ ), meeting the study's primary endpoint. Several secondary endpoints were reached as well, including a significant decrease in the risk of cardiovascular death by 30% ( $p=0.03$ ) with Multaq plus standard therapy. Multaq also significantly decreased the risk of arrhythmic death by 45% ( $p=0.01$ ) and there were numerically fewer deaths (16%) from any cause in the Multaq group compared to placebo ( $p=0.17$ ). First cardiovascular hospitalization was reduced by 25% ( $p=0.000000009$ ). Treatment was well tolerated with an adverse event profile similar to placebo. Based on the results Sanofi-Aventis plans to submit an MAA with the EMEA and an NDA with the FDA in the third quarter of 2008.

### Gastroenterology


■ **Salix** reported positive results from a phase IIb trial of **rifaximin** for the treatment of

diarrhea-associated irritable bowel syndrome (d-IBS). This multi-center, double-blind, placebo-controlled, randomized trial enrolled adult subjects who received rifaximin 550 mg twice daily or placebo for 14 days, followed by an additional 14 days of placebo in both groups and a 12-week follow-up phase. The co-primary endpoints were adequate relief of global IBS symptoms (SGA) and adequate relief of bloating (BL) compared to placebo. Both endpoints were reached, with a significant improvement over placebo in SGA (52% versus 44% respectively,  $P=0.03$ ) and adequate relief of BL (46% versus 40%,  $P=0.04$ ). Response was sustained up to 12 weeks after treatment was discontinued. Rifaximin improved both SGA and BL in equal to or greater than four weeks ( $p<0.05$ ), during all four weeks ( $p=0.02$ ), and at Week 3 ( $p<0.02$ ) and Week 4 ( $p<0.02$ ). At Week 4 (end of treatment phase) subjects in the rifaximin arm achieved relief of SGA (53%) and BL (50%) compared to 43% and 42% of subjects in the placebo arm, respectively ( $p=0.01$ ). At the end of the 12-week follow-up, rifaximin treatment resulted in an improvement in SGA versus placebo (62% versus 49%, respectively;  $p<0.05$ ) and BL (59% versus 51%, respectively;  $p<0.05$ ). Treatment was well tolerated with an adverse event profile comparable to placebo. Based on the results Salix plans to pursue FDA approval of rifaximin for this indication.

■ **Tioga** released positive results from a phase IIb trial of **asimadoline** for the treatment of

irritable bowel syndrome (IBS). This randomized, double-blind, placebo-controlled, dose-ranging study enrolled 596 subjects with diarrhea-predominant IBS, constipation-predominant IBS and alternating IBS. The subjects received asimadoline 0.15 mg, 0.5 mg or 1.0 mg tablets or placebo twice daily for 12 weeks. The primary endpoint was number of months a subject was a responder for adequate relief of pain. Secondary endpoints included adequate relief of IBS symptoms and straining. Benefit in subjects with D-IBS and A-IBS was observed while no benefit was observed in the C-IBS group. The subjects with D-IBS with at least moderate pain achieved a 27% improvement in the percent number of months with adequate relief of IBS pain compared to placebo (47% versus 20%,  $p=0.011$ ) with the 0.5mg dose of asimadoline. A 25% increase in pain free days was seen with 0.5 mg asimadoline as compared with placebo ( $p=0.001$ ). Statistically significant improvement in pain was seen by Week 3 and persisted for the duration of treatment ( $p<0.05$ ). Statistically significant improvements over placebo were seen at the 0.5 mg dose of asimadoline in the following secondary endpoints: urgency, adequate relief of IBS symptoms, stool frequency, bloating and daily pain. At the 1.0 mg dose of asimadoline statistically significant improvements were seen in the secondary endpoints of urgency, adequate relief of IBS symptoms, bloating and daily pain. The subjects with A-IBS with at least moderate

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## Trial Results (continued from page 8)

pain achieved a 23% improvement in the percent number of months with adequate relief of IBS pain compared to placebo (50% versus 27%,  $p=0.022$ ) with the 1.0 mg dose of asimadoline. Statistically significant benefit was also seen in the secondary endpoint of adequate relief of IBS symptoms at the 1.0 mg compared to placebo (57% versus 33%,  $p=0.032$ ). Based on the results Tioga plans to continue with the development of asimadoline.

### Musculoskeletal

- **Amgen** released positive results from a phase III trial of **denosumab** for the treatment of postmenopausal osteoporosis. This randomized, double-blind, active controlled, parallel group study enrolled 504 women with low bone mineral density (BMD) who had previously been treated with alendronate (Fosamax). The subjects received denosumab treatment (60 mg twice yearly) or continuing alendronate therapy (70 mg weekly) for 12 months. The primary endpoint was the effect of denosumab treatment on total hip BMD when compared to continuing alendronate therapy at 12 months. The primary endpoint was reached; the relative magnitude of BMD improvement at the total hip was approximately 80% greater in the denosumab versus the alendronate group. The secondary endpoints were reached as well, with significant BMD gains at all sites measured including lumbar spine, femoral neck, distal radius, and hip

trochanter compared with the group that continued on alendronate. Adverse events were comparable between the treatment arms. Based on the results Amgen plans to continue with the development of denosumab.

### Neurology

- **Eisai** issued results from a clinical study of **rufinamide** for the treatment of Lennox-Gastaut syndrome (LGS). This multi-center, double-blind, placebo-controlled, randomized, parallel-group study enrolled 139 subjects between the ages of four and 30 years who were being treated with one to three concomitant stable dose antiepileptic drugs (AEDs). The subjects received either rufinamide (titrated up to 45mg/kg per day) or placebo in addition to their other AEDs. The trial met all the primary endpoints. The median percentage reduction in total seizure frequency from baseline was greater in the rufinamide therapy group than in the placebo group (32.7% versus 11.7%;  $p<0.002$ ). The rufinamide-treated subjects had 42.5% median percentage reduction in tonic-atonic seizure (drop attack) frequency per 28 days from baseline as compared with 1.4% increase in the placebo-treated subjects ( $p<0.0001$ ). The rufinamide group had a statistically significant improvement in seizure severity ( $p<0.005$ ) and a higher percentage of subjects who experienced at least a 50% reduction in tonic-atonic seizure frequency per 28 days compared with placebo (42.5%

versus 16.7;  $p=0.002$ ). Treatment was generally well tolerated. An NDA for rufinamide is currently under review.

### Oncology

- **Novartis** reported positive results from a phase III trial of **everolimus** for the treatment of renal cell carcinoma (RCC). This randomized, double-blind placebo-controlled multicenter trial, dubbed RECORD-1 (REnal Cell cancer treatment with Oral RAD001 given Daily), enrolled 400 subjects with RCC whose cancer worsened despite prior treatment. The subjects received everolimus or placebo in combination with best supportive care (BSC). The primary endpoint was progression-free survival. This was reached with statistical significance over placebo, with a median progression-free survival of four months versus 1.9 months, respectively ( $p<0.0001$ ); the risk of cancer progression was reduced by 70% ( $p<0.0001$ ). There was no significant difference between everolimus and placebo in the main secondary endpoints of overall survival ( $p=0.23$ ) and objective response rate (1% versus 0% of responders). However, in a group of subjects evaluable for best percentage change in target lesions, tumor shrinkage was observed in 50% of subjects receiving everolimus during the double-blind portion of the study versus 8% of subjects receiving placebo. Based on the results, Novartis plans to file an NDA with the FDA in the second half of 2008.

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## Biotech Review

### From *BioWorld Today*

- Shares of **lomai** surged more than 117% after the firm agreed to be acquired by Austrian vaccines maker **Intercell** in a deal valued at about \$189 million.

Intercell's bid of \$6.60 per share marked a hefty premium—about 126%—to lomai's May 12 closing price of \$2.92, though it still fell short of the company's February 2006 initial public offering price of \$7. But the deal provides a much-needed boost for lomai, which ended 2007 with only \$15.5 million in the bank.

That, plus its grants and government contracts relating to its pandemic influenza vaccine adjuvant, were projected to carry the company no further than the third quarter of this year.

- **Osiris Therapeutics** said it plans to sell its Osteocel business to **NuVasive** for \$35 million in an upfront payment at the closing of the deal, and up to \$50 million in future milestone payments. In a separate agreement worth up to an additional \$52 million in revenue to Osiris, the company will manufacture and supply NuVasive with Osteocel for up to 18 months. Osteocel, which preserves the native stem cell population in marrow-rich bone, is used in spinal applications for bone regeneration. The money will help fund clinical trials of Prochymal, Osiris' most advanced product, which is being evaluated in graft-vs.-host disease, Crohn's Disease and acute

myocardial infarction. In addition, the company is developing follow-on versions of Prochymal under a Defense Department contract worth \$224.7 million, for acute radiation syndrome. Another product Chondrogen for arthritis of the knee is entering phase II/III testing.

- A bipartisan group of lawmakers introduced legislation in both chambers of Congress that would provide \$200 million in federal funds for research and discovery of treatments for brain-related injuries and illnesses. The **National Neurotechnology Initiative Act** is designed to increase the speed at which new therapies reach the U.S. market. The legislation would boost current federal funding by \$75 million for small biotech and other companies targeting therapies for brain-related illnesses and injuries. It also would provide \$80 million to the National Institutes of Health to improve its neuroscience infrastructure and \$30 million to the FDA for hiring new medical review officers for neurological-related products and other activities.
- With its lead cell therapy program in a pivotal study, **Aldagen** has decided to brave the public markets. The Durham, N.C.-based firm filed for an initial public offering, aiming to raise as much as \$80.5 million in gross proceeds to support ongoing research

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and development work, manufacturing improvements, potential commercialization of its first products and for other general corporate purposes. The company has not yet determined the number of shares to be offered or share price. Aldagen is seeking a Nasdaq listing under the ticker "ALDH." Aldagen is the seventh biotech to file for a U.S. IPO in 2008—there are a total of 17 pending IPOs, according to BioWorld Snapshots—and like the others, the company faces the daunting challenge of squeezing out the narrow IPO window. In its prospectus, Aldagen said proceeds from the offering are expected to be used in part for ongoing research and development activities, including clinical trials. The firm develops cell therapy treatments based on its platform technology, which uses adult stem cells expressing high levels of aldehyde dehydrogenase (ALDH), an enzyme believed to help promote regeneration of multiple types of cells and tissues. Aldagen's technology is used to isolate the stem cells with high ALDH levels, known as ALDH-bright cells, for therapeutic use.



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