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# START-UP



Windhover's Review of Emerging Medical Ventures

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## PANACEA

## PHARMACEUTICALS INC.

*A multi-platform approach for detecting changes associated with CNS diseases*

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- **Contact:** Hossein A. Ghanbari, PhD, president and CEO
- **Industry Segment:** Biotechnology
- **Business:** Diagnostics & therapeutics for neurodegenerative diseases, cancer
- **Founded:** April 1999
- **Founders:** Hossein Ghanbari, Kasra Ghanbari
- **Employees:** 10
- **Financing to date:** \$1.5 million

- Scientific and Clinical Advisors:
- **Clinical:** Christopher Kircher, MD (Riverhills Healthcare Inc.); William Summers, MD (Alzheimer's Corp.)
- **Scientific:** Garth Bissette, PhD (University of Mississippi); Suzanne de la Monte, MD (Brown University); Allan Goldstein, PhD (George Washington University); George Perry, PhD (Case Western Reserve University); Mark Smith, PhD (Case Western Reserve University); Jack R. Wands, MD (Brown University); Benjamin Wolozin, MD, PhD (Loyola University Medical School)

**T**hey were early participants in **Nymox Pharmaceutical Corp.**, a developer of therapeutics and diagnostics for Alzheimer's disease. Now father-and-son team Hossein and Kasra Ghanbari have reunited at **Panacea Pharmaceuticals Inc.**, which is assembling protein-based technologies for detecting and identifying changes associated with and involved in diseases of the central nervous system.

Panacea's programs encompass brain cancer diagnostics and therapeutics, diagnostics for transmissible spongiform encephalopathies, and therapeutics for Alzheimer's disease and Parkinson's disease. While development of therapies for Alzheimer's disease remains a focus for Panacea, the founders expect other programs to move more rapidly through development. Indeed, the company's development strategy has been opportunistic: the founders have assembled promising technologies identified through their experience and contacts with academics and other companies, as opposed to being impelled by a particular technology platform.

"We wanted a mix of projects, both short and long term," explains president and CEO, Hossein Ghanbari. But all of Panacea's programs share the common thread of a core competency in brain disease, including brain cancer, and neurodegenerative disorders. Also interwoven into its thinking is to only work with "best in class" collaborators, Ghanbari says, with whom he'd had some association over the past fifteen years.

Diagnostics for monitoring drug efficacy will provide the company near-term revenues. Its first program, grounded in collaborative research

and licensing agreements with Rhode Island Hospital and Brown University, is to develop an assay for the enzyme, human aspartyl (asparaginyl)-B hydroxylase (AAH), which its academic collaborators have spent more than \$6 million over five years studying, Ghanbari says. Overexpression of this enzyme correlates with more aggressive and invasive growth of tumors *in vivo* and is a consistent feature of many carcinomas. Panacea received exclusive, worldwide rights to AAH technology for all therapeutic as well as diagnostic applications in exchange for milestones, royalties, and a commitment to fund two Rhode Island Hospital researchers.

“AAH is overexpressed in the periphery of all the tumors we’ve studied,” Ghanbari notes, including brain, pancreatic, liver, breast, and colon. When placed into cells that don’t usually express it, AAH transforms them into cancer cells. And when cells that produce AAH are injected into mice, tumors form at the injection site. Now, using an anti-AAH monoclonal antibody, FB50, generated in the labs of its collaborators, Panacea is developing a test that it will use to monitor the efficacy of various drugs in clinical trials. The company will provide the assay either in its own clinical reference laboratory, for which it intends to apply for CLIA certification in the next few months, or as a home-brew test. It may also develop a screening kit in collaboration with a worldwide diagnostics player; Panacea is currently talking to a potential European and Japanese partner, Ghanbari says.

Although Panacea thinks drugs that target AAH, which is found in the periphery of tumors, could be broad-spectrum anti-cancers, it is first pursuing a therapeutic indication in brain cancer, which Ghanbari believes offers a fast route to FDA approval and the prospect of a relatively small pivotal clinical trial. When AAH production is inhibited using a Panacea biologic, PAN-346, now in preclinical development, cells revert to a non-cancerous phenotype. For other cancer types, they expect to develop small-molecule AAH regulators.

Its second program, for diagnosing transmissible spongiform encephalopathies (TSEs), which include the veterinary diseases scrapie and BSE (mad cow disease) and human TSEs Creutzfeldt-Jakob disease (CJD), kuru, and Gertsman-Straussler-Scheinker syndrome, is earlier stage.

Panacea is in the process of licensing three patents from the **National Institute of Mental Health** of the **National Institutes of Health**, Hossein Ghanbari says, covering detection of and antibodies to the protein, 14-3-3, a marker for sporadic CJD. By the end of 2000, Panacea expects to have completed development of an immunoassay that, like FB50 in cancer, will offer via its clinical laboratory service—a way to leverage the capabilities and infrastructure Panacea is developing in diagnostics. Because of the ongoing controversy in Europe over CJD and contaminated beef, he has higher expectations for making commercial inroads there with the test. “It’s not a high priority, but if there’s a demand, we’ll be there,” he says.

Of more central importance to the company are its therapeutics development programs for Alzheimer’s disease (AD) and Parkinson’s disease. “Our expertise at Panacea lies more in AD than in other areas,” Ghanbari notes, citing his ten-year stint at **Abbott Laboratories Inc.**, where he notes he developed several pharmaceuticals and the first marketed AD test, and at Nymox. He is also currently chairman of the Alzheimer’s Corp. of Albuquerque, NM. While at Nymox, his son, COO Kasra Ghanbari, participated in the development of the *AD7C* AD diagnostic test, which that company sells.

Hossein Ghanbari explains that Panacea deviates from the traditional “one drug, one disease” approach to AD and considers plaques and tangles in the brains of AD patients a histological symptom, just as cognitive impairment (memory loss) is a clinical symptom. Panacea’s approach is to treat the underlying causes of AD and not the symptoms. He explains Panacea’s drug discovery rationale: cells affected by AD often appear healthy under a microscope, but they are prone to insults, including oxidative stress. “That’s because the disease causes the cells to degenerate so they can no longer communicate with other cells.” Thus anti-oxidants like vitamin E are used as what he calls “semi-drugs” for AD.

But Panacea isn’t looking at anti-oxidants, he points out; instead, it is looking to determine why the cells are prone to oxidative stress, using novel screening methods developed at the lab of George Perry, PhD, at **Case Western Reserve University (CWRU)**, with whom it has a collaborative research agreement and a license agreement. Panacea is combining

Perry's research with its internal library of cultured olfactory neurons, which are close in behavior to neurons in the brain and which can be easily cultured *in vitro*, to devise an AD-specific cell-based model system for drug discovery.

The company is also working with a second CWRU researcher, Mark Smith, PhD, to develop a screen for AD drugs based on Smith's work in cell cycle abnormalities: neurons that reenter the cell cycle show the same biochemical and cellular changes found in neurons of AD patients. As with the Perry lab, Panacea has a collaborative research agreement and license agreement, for Smith's cell-based screening system. The CWRU connections, the Ghanbaris' experience in AD, and the strength of the company's scientific advisors position Panacea to become a leader in oxidative stress-based neurodegeneration, the company believes.

The Parkinson's disease program derives from the discovery of alpha-synuclein (ASN) and its link to the pathology of Parkinson's disease and other Lewy body (LB) diseases. LBs are neuronal inclusions that are the neuropathologic hallmark of Parkinson's disease. A team of researchers at **Loyola University Medical Center** in Maywood, IL, led by Benjamin Wolozin, MD, has shown that iron and free radical generators, such as dopamine, stimulate the production of intracellular aggregates that contain ASN and ubiquitin. These aggregates can be identified by immunocytochemistry or histological staining techniques; under a research agreement with Loyola, Panacea is collaborating with Wolozin's lab to identify and develop drugs to prevent ASN aggregation. Panacea has produced a lead, PAN-408, which it expects to take into human clinical trials in 2001.

For its first three months, Panacea operated out of Hossein Ghanbari's home office; in July 1999, the company became one of the first tenants of the Maryland Technology Development Center incubator. It has obtained over \$1.5 million in funding, including \$900,000 of a \$1.4 million Series A round; Ghanbari hopes to raise another \$5-10 million in a Series B financing by year-end.

In the next 12 months, Panacea hopes to begin marketing its cancer diagnostic, file an Investigational New Drug application for PAN-346

in brain cancer, identify a preclinical pancreatic cancer product candidate, and conduct preclinical studies for Parkinson's therapy. Shortly after that, it will decide on preclinical candidates for AD therapy.

Seven years prior to co-founding Panacea, Hossein Ghanbari had been co-founder and SVP, R&D, of **Molecular Geriatrics Corp.** After that, he was SVP for R&D and strategic planning at Nymox. Kasra Ghanbari was Nymox's project leader for Alzheimer's diagnostic development, director of laboratory and technical operations, and scientific and technical director of its clinical reference lab. Alan Deutch, PhD, VP for business development, was most recently director of strategic ventures and licensing at **Specialty Laboratories Inc.** Sherri Bale, PhD, is director of Panacea's clinical reference lab. She is co-founder, president and clinical director of **GeneDx Inc.**, which provides genetic testing services. Her management experience also includes 16 years at the NIH. CFO James Matthew spent 20 years with KPMG, most recently as managing director, global transactions services, for its investment banking practice. He is currently CFO and managing director of Angel Capital Network Inc., in northern California.



—MLR