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Reason for report:

INSIGHTS AND OUTLOOK

HEALTHCARE STRATEGY

Leerink U. Charts Course of Healthcare Investing

• **Bottom Line:** We recently hosted Leerink University, a two-day deep dive into the factors for successful healthcare investing. We looked at tightening regulatory and reimbursement issues and the uncertainties of healthcare legislation. On a more positive note, we identified investment opportunities in emerging technologies and emerging markets. Overall, the message was that innovation will continue to be rewarded and drive healthcare investing. Please read on and join us at Leerink University.

• **The FDA pendulum has swung toward emphasizing risk (safety) over benefit (efficacy).** In Therapeutics, the increasingly risk-averse environment is leading to higher costs, longer timeframes and increased risk of final approval. In Diagnostics and Medical Devices, there may be changes in the regulatory pathway, leading to similar results. Innovation will still be rewarded, but it could take longer.

• **Identifying alpha in Biotech Binary Investing.** At Leerink U., we presented the findings of our analysis of 159 events over 2008-09. We found that the best time to invest for binary events is 90 days prior to an event, and it has been more attractive in 2009 than in 2008, benefiting from a rising tide. Commercialization risk is different than binary event risk, and we suggest selling post positive regulatory events to avoid underperformance.

• **Leading life sciences venture capitalists offered strategies and ideas for finding long-term healthcare growth opportunities.** LU attendees heard from top venture investors that exciting long-term growth could be found in life science technologies, molecular diagnostics, HCIT and therapeutic development platforms; an expert presentation on healthcare in emerging economies highlighted China as likely to provide a macro setting for successful healthcare and life science industries.

• **Healthcare reform is still uncertain.** Even with the latest CBO scoring, HC reform is not a done deal. But, whatever passes, the Leerink University consultant felt that it would be positive for healthcare stocks. Net-net, about \$1 trillion will be added to healthcare expenditures, positive for HMOs and hospitals.

• **Looming Medicare changes also a concern.** The Leerink University speaker sees increased emphasis on costs, exemplified by recent proposals for an increased MedPAC role and dialysis bundling. These show a shifting priority toward payment for outcomes, not procedures, which will require HCIT to implement.



LEERINK SWANN

HEALTHCARE EQUITY RESEARCH

S&P 500 Health Care Index:

332.28

Companies Highlighted:

ABT, ACOR, ALXN, AMGN, ARIA, BAX, BCR, BSX, CELG, CERN, CI, CVH, CYH, GENZ, GILD, HGS, HMA, HUM, ILMN, IMA, ISPH, JNJ, KG, LPNT, PFE, SHPGY, THC, UHS, WLP

Please refer to Pages 15 - 17 for Analyst Certification and important disclosures. Price charts and disclosures specific to covered companies and statements of valuation and risk are available <https://leerink.bluematrix.com/bluematrix/Disclosure2> or by contacting Leerink Swann LLC Publishing Department, One Federal Street, 37th Floor, Boston, MA 02110.

FDA: Increasing Conservatism & Oversight the Watchwords

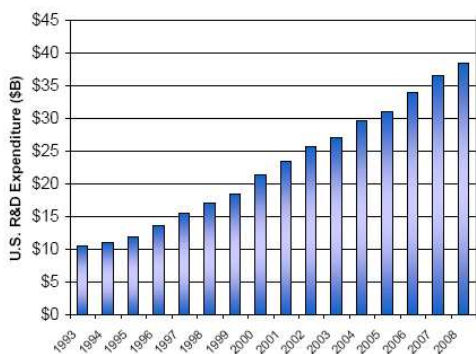
The pendulum has swung at the FDA. The five essential FDA principles are safety, efficacy, comparative efficacy, data, and an assessment of benefit/ risk. New leadership at the FDA is accelerating the shift toward emphasizing Risk (safety) vs. Benefit (efficacy), according to MEDACorp consultants who presented at Leerink University.

Therapeutics: Safety is an ever more primary concern in this area. It is an increasingly conservative climate for new drug reviews. According to a MEDACorp consultant who was previously with the FDA, there is especially heightened scrutiny on areas with problems in the past, such as cardiovascular events, liver toxicity, QTc, and suicidality. The FDA is increasing its emphasis on compliance and enforcement. This is leading to:

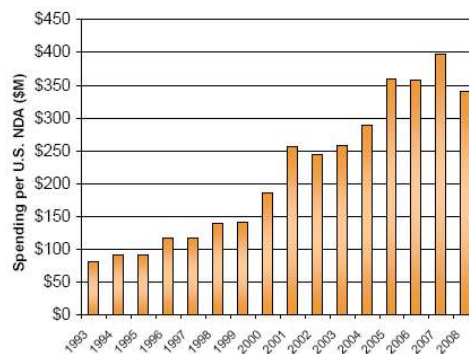
- Increasing requests for pre- and post-approval safety studies.
- Increasing focus on data quality, integrity and conduct of clinical trials.
- An increasing number of Advisory Committee meetings since 2007.
- Increasing post-marketing safety requirements.
- Increasing use of REMS (Risk Evaluation & Mitigation Strategy). These post-approval programs are for products with serious safety concerns and may include patient registries.

Investment Implications in Therapeutics. This increasingly risk-averse environment is leading to higher costs, longer timeframes, and increased risks of final product approval. Already, R&D costs have been rising faster than the number of new drugs approved, leading to higher R&D costs per drug.

U.S. R&D expenditures

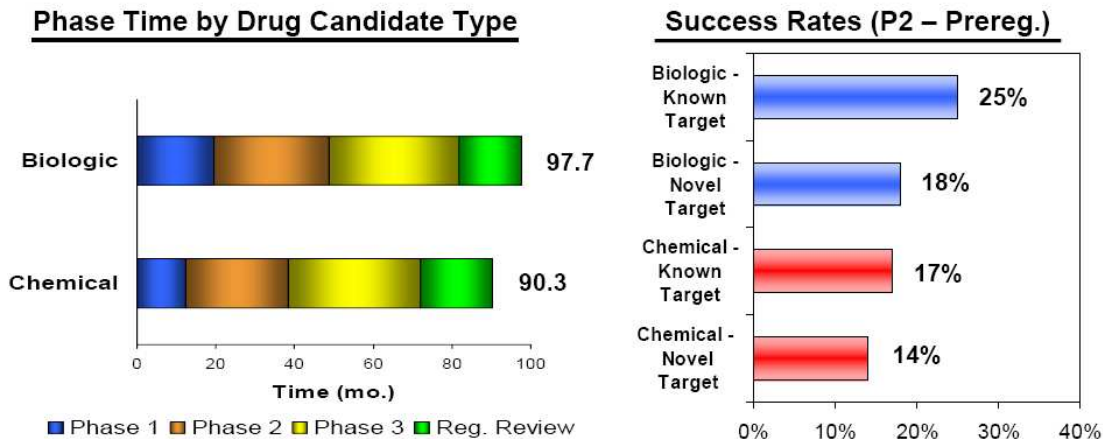


Ratio of R&D expenditures to NDA submissions



(L) Expenditures by PhRMA-member research-based pharmaceutical companies
 (R) Ratio of PhRMA member total R&D spend to total NDA submissions to FDA
 Sources: PhRMA. PAREXEL

Biologics take longer to develop, but are more likely to succeed because of their targeted approach.



Sources: EvaluatePharma, Tufts Center for the Study of Drug Development (2006). PAREXEL (2009): success rate data encompass 2002-2007

We view large cap Biotechs as attractive, especially since they have underperformed year-to-date. Our two favorite large caps are Outperform-rated **GILD**, which has a best-in-class HIV franchise and **CELG**, whose Revlimid is emerging as a dominant franchise in cancer.

Smaller Biotech stocks that our sector analysts favor include **ACOR**, **ALXN**, **ARIA**, **HGSI**, and **ISPH**. Specialty pharma companies can also provide attractive innovative products. Here our sector analyst favors **KG** and **SHPGY**.

Lastly, Large Pharma stocks have also underperformed YTD. Closing of pending mergers should allow traditional healthcare investors to return to these arbitrage situations. Lifting the legislative cloud of healthcare reform may also spur investors to look again at **PFE**, our favorite large-cap Pharma stock.

Diagnostics: IVD-MIA area of continued interest to the FDA; CLIA pathway to market controversial to some. New FDA leadership may change how new and complex diagnostic products are regulated. Recent industry presentations from the Office of In Vitro Diagnostics (OIVD) officials suggests a growing level of interest and scrutiny specifically in next-generation genetically-based diagnostics. There is lots of public pressure on the FDA to do something soon.

Diagnostics' traditional dual paths to market are under scrutiny. Currently, diagnostics can be approved under PMA/ 510(k) (FDA) or CLIA (CMS) regulations. In recent years, there has been a rising level of concern from FDA regarding IVD-MIAs due in part to the complexity of these tests. Many novel diagnostic tests are no longer as simple as a basic glucose test supported by a body of literature. Increasingly, today's cutting-edge diagnostics combine poorly understood biomarkers and inaccessible informatics.

Defining “IVD-MIA” (also known as lab-based tests)

- IVD Multi-variant Index Assays are defined as “products that combine the values of multiple variables using an interpretation function to yield a single, patient-specific result that is intended for use in the diagnosis of disease or other conditions...and provide a result whose derivation is non transparent and cannot be independently derived or verified by the end user.”

Defining “CLIA”

- Clinical Laboratory Improvement Amendments
- Covers 200k lab entities, regulated by CMS (not FDA)

Defining 510(k) Submissions

- Section 510(k) of the Federal Food, Drug, and Cosmetic Act has review time of 90 days in order to market a device that’s “substantially equivalent” to one already on the market.

Defining PMA

- If a device is sufficiently different, it undergoes a PMA (pre-market approval), which requires more data, maybe an FDA Advisory panel, and a review time usually 180-320 days.

Source: Leerink Swann LLC Research, www.FDA.gov

Storm clouds forming. In the past six months, a new FDA commissioner and director of OIVD have been appointed. Recently, the FDA launched an evaluation of the 510(k) process, while the new director of OIVD has taken a hawkish, pro-regulation stance in diagnostics and may address IVD-MIAs. We will likely see a long-term broader move by FDA to bring all tests under its regulatory purview. Meanwhile, industry is pursuing several strategies to dictate what the new regulatory framework will look like.

- Some companies are rushing to launch new tests under CLIA, hoping a grandfather clause will be enacted.
- Some are launching CLIA tests while running clinical trials in parallel as backup.
- Others are lobbying Congress to raise standards quickly.

Companion Diagnostics also raising FDA concerns. Companion Diagnostics are IVD tests that qualify a patient for treatment with a particular drug. Examples are the HER-s/neu assay required prior to treatment with Herceptin, and GHDX’s Oncotype Dx test that predicts outcome, both for breast cancer. We expect a more straightforward regulatory pathway for well-pointed companion diagnostics, which would be easier if it’s for a single marker and single drug. Approval will be harder if it functionally changes a drug label.

Personal Genomics Services may also see increased FDA oversight. These are currently offered by 23andMe, Navigenics, and **ILMN** (Outperform) direct to consumers. The DTC aspect may create a concern, due to the risk of misinterpretation of data and potential confusion among customers and the general public. We expect more involvement from the FDA, with initial comments over the next 6 months, but no formal action until perhaps 2011.

Investment Implications in Diagnostics. Molecular Dx is the fastest growing segment of the Diagnostics market, growing 15-20% annually vs. 6-7% for the larger pie. Changing regulatory oversight could lead to increased time to market and higher development costs, but at the same

time erect barriers to entry against competitors. In Diagnostics, our sector analyst favors **IMA**. We believe IMA can post improving sales performance and better-than-expected operating profitability as the company integrates its numerous acquisitions. We expect respectable point-of-care (POC) and pregnancy testing trends to help IMA post solid growth in both its consumer and lab diagnostics businesses, while de-emphasizing its nutritional business.

Medical Devices may see changing Regulatory Requirements – 510(k) vs. PMA. The FDA review process for medical devices is facing scrutiny as well. After a January Government Accounting Office (GAO) report evaluating the FDA's 510(k) clearance process, on 9/23/09, the FDA announced "it has commissioned the Institute of Medicine (IOM) to study the premarket notification program used to review and clear certain medical devices marketed in the United States". An internal FDA memo said: "It's Autumn, and change is in the air. This is particularly true for our 510(k) program" (*WSJ, 9/30/09*). We view this as a catalyst for long-term change which can lead to delays in product approvals.

At Leerink University, a MEDACorp consultant previously with FDA said this could lead to:

- Increased requirements for premarket testing
- Increased requirement for clinical data in 510(k)s
- Scientifically rigorous clinical trials for 510(k)s
- Increase in number of "Not substantially equivalent" decisions, leading to more PMAs for innovative products

With Enforcement and Compliance also on the Rise, this MEDACorp consultant sees more:

- More frequent inspections, both routine and "for cause"
- Increased scrutiny of post-approval or postclearance device modifications
- Increased scrutiny of medical device surveillance (i.e., MDR)
- More aggressive action regarding off-label use

Combination products are also under a microscope. Examples of such products are drug-eluting stents, antimicrobial coated implants, catheters, and bandages, dermal replacement devices with living cells, and drug delivery devices such as pumps. The MEDACorp consultant expects fewer combo devices will be approved under the 510(k) pathway.

Off-label use may also get scrutiny from the DOJ in conjunction with the FDA. The MEDACorp consultant cited biliary stents for peripheral vascular use. Our Leerink Swann sector analyst indicates such stents are made by all major Medical Devices companies, **ABT, BCR, BSX** and **JNJ**, but would be a very small revenue contributor to all.

Investment Implications in Medical Devices. Our Leerink Swann Medical Devices analyst, Rick Wise, says that increased regulatory scrutiny and a review of the 510-k program could lead to slower approvals and more product delays. Our top picks in the sector remain Outperform-rated **BSX** and **BAX**. At BSX, we have high confidence the new CEO should help drive positive

operating leverage, balance sheet improvements and better execution. We continue to expect BAX to comfortably meet or exceed the company's long-term growth goals driven by an expanding portfolio of higher-margin products and further operating leverage due to both positive mix shifts and greater operating efficiencies.

Binary Event Investing

At Leerink University, one of Leerink Swann's Biotechnology analysts, Josh Schimmer, presented the conclusions from our report "*Trends in Biotech Binary Event Investing: Identifying Alpha*". This report identified potential patterns caused by investor sentiment around binary events that can result in alpha. This historical analysis took a deep dive, assessing key clinical and regulatory binary events from January 1, 2008 until September 15, 2009. Combined with deep fundamental analysis & selectivity, we believe this approach can drive meaningful outperformance.

The best time to invest for binary events is 90 days prior to an event. As events get closer, investor interest increases, more often than not resulting in positive alpha before an event. In our opinion, the returns seen in the 90 days leading up to an event are not only significant, but persistent.

Binary event investing, overall, has been more attractive in 2009 than in 2008. Upside for positive events, on average, has been greater in 2009 vs. 2008 across all investment horizons, without greater downside for negative events. And there has been more room to outperform following events with both positive and negative outcomes. This positive skew illustrates the benefit of investing in binary events when a rising tide is lifting all boats.

2008	Alpha Relative to NBI								
	-180	-90	-30	-5	0	+5	+30	+90	+180
All Events %	0.0	3.0	3.0	2.2	0.0	1.0	-0.1	-1.7	-2.0
Positive Events %	-7.1	-4.9	2.1	-0.5	18.7	3.5	4.5	2.7	-4.0
Negative Events %	7.0	10.2	3.8	4.7	-16.5	-1.1	-4.2	-5.5	0.5
Probability of Positive Return	49%	62%	56%	49%	48%	52%	49%	51%	42%
Probability of Negative Return	51%	38%	44%	51%	52%	48%	51%	49%	58%

2009	Alpha Relative to NBI								
	-180	-90	-30	-5	0	+5	+30	+90	+180
All Events %	32.1	30.3	10.6	2.0	10.3	2.1	3.6	14.3	8.9
Positive Events %	37.1	40.5	14.2	3.2	36.1	3.1	5.0	5.2	4.3
Negative Events %	27.4	20.8	7.2	0.8	-13.8	1.3	2.3	20.4	13.4
Probability of Positive Return	60%	70%	56%	57%	48%	44%	55%	49%	56%
Probability of Negative Return	40%	30%	44%	43%	52%	56%	45%	51%	44%

Source: Leerink Swann, StreetAccount, FactSet

"Buy on the News" Strategy only Worked for Small Cap Names. Small-cap stocks rose after positive events and even showed positive alpha by days 90 and 180 post negative events. Mid- and large-cap stocks have more dramatic sell-offs following positive binary events.

Phase II Better Risk/Reward than Phase III. Risk/reward, especially for small-cap companies, is favorable both before and after top-line Phase II data releases. In Phase III, less than tolerable safety concerns or lackluster efficacy can send a stock tumbling.

Own it Into FDA but Be Careful Coming Out of FDA. In particular, buying small-caps 90 days prior to regulatory events produced the largest alpha with a high probability of positive outcomes.

Commercialization Risk is Different than Binary Event Risk. As investors focus turns from approval toward commercialization, new questions often are raised, regarding addressable market, marketing strategy and capability, and competitive landscape. This more often than not results in a sell-off. We suggest selling post positive regulatory events, while post negative events performance is mixed.

For a complete methodology and list of upcoming events, see our note “*Trends in Binary Event Investing: Identifying Alpha*”, published October 1, 2009.

LU Sessions Detail Future Opportunities for Healthcare Investors

Two sessions at Leerink University focused on long-term considerations and opportunities for healthcare investors. Invited speakers from the venture capital industry outlined their processes and areas of interest for the public market investors in attendance.

We came away from the sessions more informed about and appreciative of long-term opportunities in molecular diagnostics, life science platforms, next-generation therapeutics, HCIT and services, and in emerging geographic markets. We heard about the importance of proprietary assets like intellectual property and the desire for products and addressed large markets. As well, we heard loudly and clearly from our venture capitalist speakers that finding the right management team, and in particular the right CEO, was critical to the success of a venture-backed company. Our panelists repeatedly spoke of the value of a CEO who could grow young companies reliably.

At Kleiner Perkins, Investing in Life Science Platforms and Molecular Dx

On the Leerink University panel “Healthcare Investing’s Future”, Risa Stack from Kleiner Perkins Caufield and Byers described a process for life science venture investing at her firm that often begins with an idea without an entrepreneur. She and her partners evaluate advances in science and technology, often generating ideas for businesses that they want to fund. They then find an entrepreneur to take on the challenge of developing and commercializing their inspiration with their financial backing and guidance.

In life sciences and molecular diagnostics, Risa told attendees that improvements in technology-related fields were allowing for the creation of exciting new platforms for gathering high-density genetic information. Kleiner portfolio company Pacific Biosciences (www.pacificbiosciences.com), developing a transformative platform for high-density DNA sequencing analysis, leverages well advances in biology, biochemistry and physics. Risa described the Pacific Biosciences technology

as one that could continue to slash the cost of DNA sequencing, to the point where individuals could afford to acquire their personal genomic information and make improved healthcare decisions.

Advances over the last several years in enabling life science technologies have combined with key discoveries in genetics and molecular biology to unleash a torrent of information on genes and their relationship to disease. Risa pointed to this as a primary reason for Kleiner's interest and investments in molecular diagnostics. She sees gene-based diagnostic tests as offering an attractive investment profile: health information that enables better and more cost-effective outcomes, patent protection for test developers, and large markets. Kleiner portfolio companies like CardioDx (www.cardiodx.com), a developer of genetic diagnostic tests for cardiovascular disease, are pursuing growth markets that Risa and her partners perceive in molecular diagnostics.

Radius Ventures Likes Attractive Risk/Reward Profiles in HCIT, Services

Venture capitalist Dan Lubin of Radius Ventures (www.radiusventures.com) has an investment strategy related to healthcare and life sciences that is focused on making later-stage investments in developing companies. He prefers large markets, and views as especially attractive opportunities that are not reliant on FDA approval or Medicare reimbursement. He's attracted to the long-term opportunity in bringing information technology into healthcare, and is actively making investments in healthcare information technology (HCIT). One of his first screens in HCIT investing is to ask, "How much money does the customer save if this product is implemented?"

He sees healthcare providers as having underleveraged advances in information technology that many other industries have used to improve costs and productivity. He believes that there are areas of HCIT that can be especially useful in both controlling costs and improving patient outcomes. He sees HCIT as an area of intense interest and spending among healthcare providers like hospitals for the next decade. Radius portfolio companies like Management Health Solutions, Inc. (www.mhsinc.com), a clinical supply chain software company, are pursuing the long-term HCIT opportunity that interests Dan and his partners.

Dan's venture healthcare investments pointed toward improving cost efficiency in hospitals extend beyond software to other areas of services and to innovative hardware-based products as well. Radius portfolio company Aethon (www.aethon.com) is developing innovative and proprietary courier robots that improve the efficiency of in-hospital deliveries of clinical supplies, pharmaceuticals, food and other key materials.

At Bay City Capital, Opportunities Seen in Cutting-edge Therapeutics

Dr. Carl Goldfischer and his partners at Bay City Capital (www.baycitycapital.com) consider themselves to be investors in life sciences innovation. Bay City is an early-stage venture investor that seeks to capitalize on growth opportunities in therapeutics, devices and diagnostics. In its therapeutics investing, it seeks to fund 'big ideas' – companies that are seeking to advance cutting-edge medical science into new clinical medicine.

In therapeutics, Carl sees a backdrop favorable to small companies with innovative and productive therapeutic development platforms. With the world's largest drug companies facing the expiration of key patents protecting drug products with tens of billions of dollars in aggregate sales, attractive young therapeutics companies with promising and proprietary platforms will be an area of intense interest. Carl sees the acquisition and partnering environment remaining robust. Further, with the yields on R&D spending continuing to decline among large drug companies, Carl believes that there will be an increased appreciation of the efficiency and productivity of smaller biopharma platforms.

Carl notes continued risks faced by therapeutic developers, notably an FDA that seems to be ever more difficult to please in the clinical development process. However, he and his partners believe that innovative products and discovery platforms will continue to be rewarded in the healthcare and life sciences marketplace, with acquisition and partnership among the most likely avenues to venture investment realization.

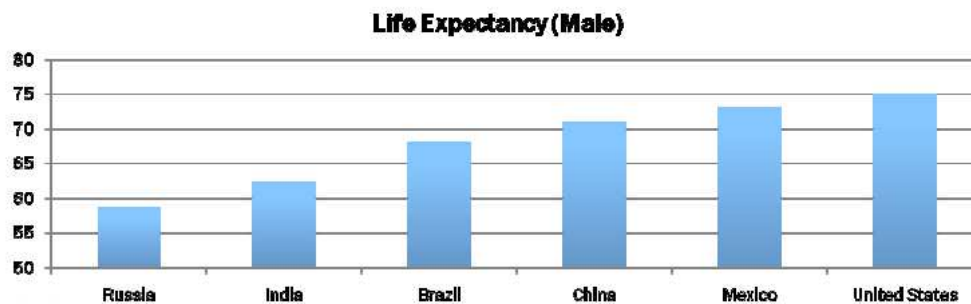
Importantly, Bay City Capital seeks in its therapeutics company venture investing sustainable innovative product development platforms as opposed to individual products. Carl and his partners would much rather invest in a technology that provides a pipeline of assets to monetize than in a single drug candidate. Bay City portfolio company BrainCells (www.braincellsinc.com) characterizes this investment approach well, capitalizing on recent discoveries proving that new neurons (nerve cells) are born in the brain not only during fetal and early development but even during adulthood. BrainCells is working to capitalize on new knowledge about neurogenesis in clinical practice with its proprietary drug discovery technology platform.

Another Bay City Capital portfolio company that illustrates the firm's investment approach well is Vivaldi Biosciences (www.vivaldibiosciences.com), a developer of novel vaccines and antivirals with increased effectiveness against seasonal and pandemic influenza. Recent discoveries in a molecule known as nonstructural protein 1 (NS1) has led to the belief that NS1-modified seasonal flu vaccines may provide improved protection. Bay City and leading researchers in this field of science founded Vivaldi. The company is currently using its drug development platform to develop a range of more potent and proprietary NS1-modified influenza vaccines.

At Kodiak, Fundamental Research Yields Emerging Healthcare Markets Opportunities

Venture investor Dr. Andrey Zarur, the head of life sciences investing at Kodiak Venture Partners (www.kodiakvp.com) is studying closely the investment opportunities presented in emerging healthcare markets like Brazil, Russia, India, China and Mexico, a group that he referred to as the BRIC-M countries. In a Leerink University session called “Healthcare in Emerging Economies”, Andrey offered LU attendees a rigorous framework for assessing private company investment opportunities in countries like these.

Country	Average	Upper 10% (E)	Lower Quart (E)
India	\$91	\$950	\$<10
China	\$277	\$383	\$250
Russia	\$583	\$1,020	\$147
Mexico	\$655	\$1,580	\$240
Brazil	\$1,520	\$2,800	\$150



Source: Kodiak Venture Partners

Andrey noted that there is not an easy answer to the question, “Should investors invest in emerging economies, and which countries?” He offered a template for formulating an answer as a function of the level of economic growth in the country, the population migration within the country from rural to urban areas, and the infrastructure for access to healthcare and the distribution of healthcare services. He also assesses the level of healthcare spending relative to GDP, in the belief that those countries with low healthcare spending as a share of GDP and high GDP growth will come to conclude that raising the level of healthcare spending is appropriate. By his template, Andrey views the best country opportunities as China, Thailand, Vietnam and Jordan.

Priority	Projected GDP Growth	Projected Migration to Urban Areas	Current HC Spend as % GDP	Infrastructure for Access & Distribution
Tier 1	High	Extreme	Low (<5%)	Very good
Examples: China, Thailand, Vietnam, Jordan				
Tier 2	Moderate to High	Moderate	Low to moderate (5-7%)	Moderate to good
Examples: India, Brazil, Chile, Korea				
Tier 3	Negative to Low	Limited	Low to moderate (5-7%)	Limited to good
Examples: Mexico, Argentina, Russia				

Source: Kodiak Venture Partners

Andrey detailed opportunities in China more specifically. With 20% of the world's population and just 1.5% of the world's healthcare spend, China is to date underspending on healthcare for its people. Accelerated economic growth is putting pressure on the current healthcare system, and the migration rate from rural to urban areas is high. He called pharma and biotech the most interesting areas of healthcare investment in China, with the industry growing at a 16% CAGR. He also called investors' attention to the rapidly expanding private hospital industry in China.

Andrey outlined several public market opportunities for investors looking to initiate or expand exposure to healthcare in China. He called SinoPharm (1099.HK), the China National Pharmaceutical Group, especially interesting. He also noted United Family Hospitals (Chindex), the first for-profit clinical chain to draw foreign capital into China. Leerink Swann does not currently include these companies in its universe of research coverage.

Healthcare Reform Still Uncertain

One of the Leerink University sessions provided a Washington update from a MEDACorp consultant who is a specialist in the analysis of significant health policy and market changes and previously was the chief operating officer of a health and group benefits insurer. The discussion focused on the impact of likely healthcare reform scenarios on HMO and hospital profitability, the softening of the individual mandate, and the bumpy road ahead before healthcare reform can get passed.

Not a Done Deal. According to the consultant, there is still a good chance that reform fails because of lack of agreement on major provisions and weak public support. The individual mandate is likely to be toothless and subsidies to purchase insurance likely modest to keep the cost of the bill down, which will lead to a bill that costs nearly \$1 trillion and only increases the

percentage of the population that has coverage from 85% to approximately 90%. Getting support for this type of bill could be a challenge.

We note that the amended Senate Finance health reform bill passed a crucial test this week when the CBO scored it as reducing the federal deficit over 10 years by \$81B and leading to 94% of the population having coverage by 2019 (the same percentage as the original Senate Finance bill). This news reduces the chances of the bill getting killed immediately.

Financing Disagreement Unresolved. The House bill partly funds reform through taxes on the rich, while the Senate Finance Committee (SFC) bill relies on taxing rich health plans. The consultant believes that the unions will kill the health plan tax and that the AMA will push for more than the one year Medicare payment fix currently in the SFC bill, creating a nearly \$500B gap that needs to be filled.

A Toothless Individual Mandate. As happened in Massachusetts, the consultant believes that Congress will exempt a lot of people from penalties if they don't buy health insurance, because it will be unaffordable to many middle class families. A weak individual mandate will lead to fewer people getting coverage and could disrupt underwriting in the small group and individual market if combined with guaranteed issuance.

The Public Option. The consultant believes that Democrats don't have the votes for a public plan, although a triggered public plan is possible as the White House has been working behind the scene to gain moderate support for it.

Investment Implications – Healthcare Reform Favorable for Industry Profits

- **Net-net, HC Reform Good for Managed Care.** The consultant believes that managed care companies can more than offset new fees, taxes and cuts to Medicare with new revenues from the 20 million newly insured and the expansion of Medicaid programs.
 - **HMO math: revenue opportunity = \$1 trillion** (federal subsidies of \$500B + \$200B from individuals + \$300 Medicaid expansion).
 - Offsets would be Medicare Advantage cuts (already softened by Senate Finance to \$123B and inclusion of a grandfather amendment) and underwriting reforms – **still a windfall for managed care.**
 - Over time, healthcare exchanges are likely to increase competition in the individual market; the small group market is already very competitive.
 - A minimum MLR of 85% is not a problem if small group and individual markets are merged.
 - According to the consultant, **CVH, HUM** and **WLP** could see some disruption. We rate CVH and HUM Market Perform, and prefer Outperform-rated WLP. The company with the least risk to cuts/underwriting risk is **CI**, which focuses primarily on the large employer market. We rate CI Outperform and it's our top pick in Managed Care. We believe all of the HMO's will trade higher once the healthcare reform overhang is removed.

- **Hospitals Benefit Too.** While the industry has committed to \$150 billion in Medicare cuts over 10 years, it is likely to receive at least double that in new revenue from newly insured patients and reduced uncompensated care. The benefits would apply equally to all public companies. We rate **CYH, HMA, LPNT, THC** and **UHS** Market Perform.

Medicare Reimbursement a well-oiled machine but changes coming

A MEDACorp legal consultant with extensive CMS (Centers for Medicare & Medicaid Services) experience provided an overview of Medicare reimbursement, which is a well-oiled machine by government standards. But focus on healthcare costs is leading to proposed changes.

Medicare Basics. Medicare covers 45M Americans and represents 13% of the federal budget and 19% of national health expenditures in 2009. The program is structured as a guaranteed benefit, with services provided by private parties paid by the government. Keys to understanding Medicare's impact on products and services are 1) Is it covered?, 2) How much does Medicare pay, and 3) How is this changing? Medicare is on an unsustainable financial path and needs to move to a more financially stable model.

Expect a broader role for MedPAC. The Medicare Payment Advisory Commission is an independent Congressionally-established 17-member body that makes recommendations to Congress and the Administration. These are advisory only, but their input is given great weight. The Obama administration has recommended giving MedPAC dramatically enhanced power, by sending their recommendations directly to the President for approval in entirety. In order to effect a change, Congress would have to pass a resolution of disapproval, subject to Presidential veto. This would lead to a dramatic shift of power from the Legislative to the Executive Branches. Moreover, the MEDACorp Washington consultant said Senators don't want to cede control to MedPAC since this is a big part of how they raise campaign funds.

Bundling creating major challenges. CMS is in the process of implementing a MedPAC recommendation to bundle products into the payment system for ESRD (End-Stage Renal Disease), which is fully-funded by Medicare. The goal is to meaningfully reduce drug spending for dialysis patients. In addition, a MEDCAC (Medicare Evidence Development & Coverage Advisory Committee) is scheduled to review drug use in the predialysis setting in March 2010, for a potential national coverage decision. As the CMS bundle is phased in, MEDACorp consultants believe cost will become a primary driver of drug utilization in dialysis. Nephrologist consultants expect significant and rapid change in patient management following implementation in 1Q10. And the legal consultant feels bundling could serve as a template for reimbursement by CMS for other diseases and interventions, which could have long-term implications.

Investment Implications in Biotech. We believe the proposed CMS bundle should materially impact use of **AMGN's** Epo and Sensipar and **GENZ's** Renagel/ Renvela, and that the reality of this challenge is still underestimated. Moreover, the review of usage of ESAs in the predialysis setting should be an additional negative hit to **AMGN's** Aranesp not appreciated by investors. Nephrologis consultants believe price will be a key determinant of uptake for new long-acting

ESAs (AFFY/Takeda's Hematide and Roche's Mircera), and the once-monthly administration offers important cost advantages over Epo. We believe this threat to **AMGN** is also underestimated. We are not changing our estimates although as we do further industry checks, each of the lines indicated below may be at significant risk. We rate **AMGN** and **GENZ** Outperform, as we believe large cap biotech stocks are undervalued and can rally once healthcare reform is resolved.

Leerink Swann AMGN, GENZ Dialysis Product Estimates

	2009E	2010E	2011E	2012E	2013E	2014E	2015E
U.S. Epo Sales	\$2.49B	\$2.56B	\$2.45B	\$2.2B	\$2.0B	\$1.9B	\$1.75B
U.S. Epo, % Total AMGN Rev	17%	17%	16%	14%	12%	11%	10%
U.S. Sensipar Sales	\$445M	\$490M	\$500M	\$510M	\$525M	\$550M	\$575M
U.S. Sensipar, % Total AMGN Rev	3%	3%	3%	3%	3%	3%	3%
Renagel/Renvela Sales	\$726M	\$830M	\$900M	\$950M	\$1000M	\$1050M	\$500M (generic)
Renagel/Renvela, % Total GENZ Rev	16%	15%	15%	15%	14%	14%	7%

Source: Leerink Swann estimates

Other challenges from CMS. Bundling is just one of the challenges cited by this MEDACorp consultant. Increasingly, CMS is interested in payment for outcomes, not procedures. This would shift payment away from quantity to quality and reduce incentives for excessive services. This would be coupled with "pay for performance" metrics which require enhanced use of health IT, such as Electronic Medical Records.

Investment Implications in HCIT. The stimulus bill (ARRA) passed earlier this year created huge incentives for providers to invest in HCIT over the next several years. Our HCIT analyst's favorite recommendation is Outperform-rated **CERN**, which sees incremental ARRA revenue of \$2B from its existing client base, on a 2009E revenue base of \$1.7B.



Disclosures Appendix

Analyst Certification

I, John Sullivan, CFA, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

I, Alice Avanian, CFA, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.



Rating	Count	Percent	Distribution of Ratings/Investment Banking Services (IB) as of 09/30/09	
			IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	74	52.86	7	9.46
HOLD [MP]	61	43.57	2	3.28
SELL [UP]	5	3.57	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months.

The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company

For the purposes of these definitions the relevant benchmark will be the Russell 2000® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.

Definitions of Leerink Swann Ratings prior to October 1, 2006 are shown below:

Outperform (Buy): We expect this stock to outperform its benchmark by more than 10 percentage points over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform within a range of plus or minus 10 percentage points of its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark by more than 10 percentage points over the next 12 months.

For the purposes of these definitions the relevant benchmark will be the Russell 2000® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Index for issuers with a market capitalization over \$2 billion.



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