2016 BDO LIFE SCIENCES RISKFACTOR REPORT

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In the Life Sciences Industry, Innovation Challenged by Capital Markets Volatility and Public Controversy

The evolving life sciences landscape has experienced highs and lows over the past year.

Amid fluctuating market dynamics and political controversy, share prices took a turn for the worse in Q3 2015, and the downward trend continued through the first few months of 2016. High-profile concerns surrounding issues like drug pricing and overvaluation of biotech stocks have also been a significant drag on the sector, perhaps contributing to a weakened IPO market. Only eight companies priced during the first quarter of 2016—and just three of those eight posted first-day gains.

However, there is plenty of reason for cautious optimism. Despite the negative headlines, the life sciences sector remains poised for healthy global growth as the industry continues to pursue innovative solutions to worldwide problems. The Nasdaq Biotechnology Index demonstrated improved performance in March and April. The New York Times reports that, in April, $40 billion of healthcare deals were announced in a single day. In addition, our BDO IPO Halftime Report found that two-thirds (66 percent) of capital markets executives predict the healthcare sector, including life sciences, will generate the most offerings during the remainder of this year. Still, life sciences stocks hit some turbulence this Spring and, after a brief reprieve, face renewed volatility in the aftermath of the U.K.'s Brexit referendum. Brexit's long-term impact on the life sciences industry remains to be seen.

As geopolitical turmoil and the drug pricing controversy linger, the road to growth may not be a straight one. According to our fourth annual Life Sciences RiskFactor Report, the top three risks this year for the largest 100 U.S. life sciences organizations are industry competition and consolidation, regulatory hurdles and intellectual property (IP) infringement. In addition, nearly 9 in 10 (89 percent) life sciences companies cite pricing pressure as a risk — the first time the report has tracked this risk factor separately.

What has become clear in recent months is that the drug pricing issue is nuanced, without an obvious solution to measuring value. Beyond the negative publicity from the actions of certain bad actors, the shift from fee-for-service to value-based care, set in motion by the Affordable Care Act (ACA), is also forcing companies to re-evaluate how they price their products in response to new reimbursement models. What it means to tie value to outcome is still being fleshed out—and in the interim, drug manufacturers will increasingly need to justify why they charge more than their competitors based on performance. In this environment, "me-too" innovations—such as a third-to-market compound with a new biomarker—and "obscure" products with small user bases may no longer warrant a pricing premium unless the manufacturer can effectively prove improved outcomes.

The business of innovation is inherently risky—and between unprecedented pricing pressure, regulatory scrutiny and market volatility, navigating today's risk landscape is as challenging as it has ever been.

The ***2016 BDO Life Sciences RiskFactor Report*** examines the risk factors listed in the most recent annual shareholder filings of the 100 largest publicly traded U.S. life sciences companies listed on the NASDAQ Biotechnology Index by revenue. The risk factors were analyzed and ranked in order of frequency cited.

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"Amid market turbulence and a difficult IPO environment, the life sciences sector has also experienced a few bright spots in M&A activity as well as promising research and product developments. While investors appear to be more risk-averse than they were during this time last year, breakthrough innovations almost always reap dividends. But, for the time being, drug pricing remains the elephant in the room."

Ryan Starkes, Assurance Partner and Leader of the Life Sciences Practice at BDO

Unpredictable Outcomes Meets Pricing Pressure

Life sciences companies frequently struggle to achieve profitability due to the high volume of capital deployed into research and development (R&D) efforts—which can take years before paying dividends. Consistent with prior years, 68 percent cite a history of operating losses as a risk, pointing to the industry's significant investment in R&D, marketing and other necessary expenses, as well as the unpredictability of outcomes. Valuations are typically based not on profits but on sales potential. However, heightened scrutiny of drug pricing and macroeconomic factors have caused valuations to drop. But the life sciences sector may be somewhat shielded from Brexit-driven economic uncertainty—and from economic headwinds in general—since products are non-discretionary and, in many cases, lifesaving. Others worry that investors will move away from smaller companies with high clinical risk, pressured into safe-haven assets by Brexit-related volatility. While the economic impact of Britain's decision to leave the EU is hotly debated, one clear outcome is more uncertainty. Eighty-three percent of companies analyzed cite headwinds from general economic and financial market conditions as a risk.

The vast majority of life sciences organizations are also concerned about the tougher financing environment: 85 percent cite inadequate liquidity or capital as a risk factor in their annual filings. According to Bloomberg data, venture capital funding in 2016 is on pace to drop about 25 percent. Seventy-one percent of the 100 largest U.S. life sciences companies cite indebtedness as a risk, up 15 percentage points over last year.

Cyberattacks and Cyber Concerns on the Rise

Nearly 9 in 10 (89 percent) life sciences companies cite cyber risk in their annual filings, up by 19 percentage points from 2015 and 43 percentage points from 2013. Life sciences companies have access to extremely valuable data assets that can translate into big payouts for hackers. The biggest cyber threat in the life sciences industry is arguably to its intellectual property, which may fall victim to insider theft or corporate espionage. However, drug and device makers are targeted for more than their IP: Records on clinical and patient data can go for 10 times the value of credit card information in online black markets.

Cybersecurity in the life sciences industry has become increasingly urgent in recent years, with almost two-thirds of pharma companies reporting a security breach, according to a Crown Records Management survey. Cybersecurity of medical devices has also emerged as a realm of concern for regulators because of the potential impact on essential clinical performance and the extended risk to healthcare organizations in shared networks. In January, the FDA issued a new set of **draft guidance** outlining recommended steps medical device manufacturers should take to address cybersecurity vulnerabilities and minimize risk to patient safety.

The guidance on medical devices highlights the challenges of cybersecurity for the extended enterprise. Any entity in the network can be the weak link, and cybercriminals are increasingly taking advantage of weaknesses in third-party relationships to gain access to the targeted company's network. Almost all companies analyzed in the RiskFactor Report (97 percent) cite supplier, vendor and manufacturer risk.

"Data—and finding ways to monetize that data—is at the heart of life science organizations' business. While they may be a less obvious target than consumer-facing industries, sophisticated hackers are stealing critical business intelligence with larger but less straightforward financial rewards. Life sciences companies must put in place the right controls and detection mechanisms to adequately guard these critical data assets against both internal and external threats."

Shahryar Shaghaghi, National Leader, Technology Advisory Services and Head of International BDO Cybersecurity

Top 25 Risk Factors

for the 100 Largest U.S. Life Sciences Companies

2016 Rank	Risk Factor Cited in 10-K Filing	2016	2015	2014	2013
1.	Competition in industry, consolidation	100%	100%	97%	100%
1t.	Federal, state and/or local regulations	100%	100%	98%	100%
1t.	Corporate copyright, intellectual property infringement	100%	99%	98%	96%
4.	Ability to commercialize and market products	98%	99%	97%	96%
5.	FDA regulatory approvals, obligations and compliance	97%	100%	94%	94%
5t.	Supply chain, supplier/vendor and manufacturing concerns	97%	99%	100%	93%
5t.	Reimbursement from third party payers	97%	96%	85%	87%
8.	Product liability and insurance costs	96%	98%	95%	87%
8t.	Product complications, side effects, delays and recalls	96%	93%	88%	88%
10.	Legal proceedings and litigation	95%	92%	91%	84%
10t.	Ability to attract and retain key personnel	95%	91%	94%	96%
12.	Volatile financial results — revenue, profitability, stock price	94%	90%	97%	92%
13.	Threats to international operations and sales	92%	88%	71%	79%
14.	Delays or unfavorable results from clinical trials	91%	92%	87%	80%
14t.	Collaborations and relationships with other companies	91%	90%	89%	92%
16.	Pressure on pricing and cost cutting	89%	N/R	N/R	N/R
16t.	Cybersecurity, including data breaches and the ability to maintain operational infrastructure	89%	70%	61%	46%
18.	Changes in healthcare laws and regulations	86%	82%	77%	78%
19.	Maintaining internal controls, financial reporting, accounting standards	85%	87%	76%	68%
19t.	Inadequate liquidity or capital	85%	84%	85%	79%
21.	Failure to properly execute corporate strategy and growth	84%	79%	66%	69%
22.	General economic and financial market conditions	83%	91%	67%	84%
23.	Anti-takeover or change of control provisions	81%	79%	75%	66%
24.	Hazardous materials - environmental, health and safety laws	78%	81%	73%	66%
25.	Natural disasters, war, conflicts and terrorist attacks	77%	76%	56%	47%

* t indicates a tie in the risk factor ranking
** NR indicates no ranking

INNOVATION IMPEDIMENTS

100% INTELLECTUAL PROPERTY INFRINGEMENT

95% LEGAL PROCEEDINGS

91% UNFAVORABLE PRE-CLINICAL & CLINICAL TRIAL RESULTS

85% ACCESS TO CAPITAL

60% PATENT CLIFFS; GENERICS

IP Remains the X Factor

Intellectual property is highly valuable to life sciences companies protecting proprietary research, the loss of which could be extremely detrimental to their businesses. All 100 companies analyzed in this year's report cite risks related to intellectual property. Potential infringement of competitors' patents and subsequent litigation also pose significant risk, with legal fees and settlements costing millions. And while not as litigious as the high-tech industry, the life sciences sector sees a number of patent disputes turn into lawsuits. Ninety-five percent cite legal proceedings and litigation in their annual filings.

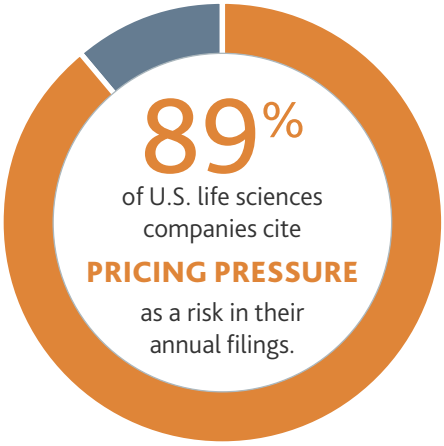
Obtaining patent exclusivity protection is a key element to the success of any life sciences company. The process can be cumbersome, time consuming and, unfortunately for life sciences companies, exclusivity expires and patents don't last forever. Once a patent has expired, low-cost generic drugs can be produced, which threaten the demand for brand-name drugs. In 2015, $44 billion of sales were put at risk by patent expirations—the highest number since 2012.

Competition Shows No Signs of Subsiding

Competition in the life sciences sector is fierce, noted as a risk by all 100 companies analyzed in this year's RiskFactor Report. Brand-name drugs have always faced competition from lower-priced generics, but innovation in the biosimilar market presents a new threat, particularly in areas like cancer treatment and rare diseases which have historically had fewer competitors. The biosimilars market is expected to reach $6.22 billion by 2020, up from $2.29 billion at the end of 2015, according to a Markets and Markets report.

As the ongoing controversy over rising drug prices highlights, industry outsiders allege a lack of competition has enabled unchecked price hikes disproportionate to the costs of production. Until recently, drug manufacturers weren't subject to market pressure to demonstrate their value. That has since changed, perhaps irrevocably. Criticism of rising prices is not new; however, the issue has received heightened—and unrelenting—attention since last summer, fueled by calls for regulatory change in the midst of the election season.

Competition for talent is another challenging frontier for life sciences companies, with 95 percent citing attracting, retaining and motivating key personnel and management as a risk factor. Compensation packages for senior biotech professionals are more attractive than ever, and many top executives can be enticed away from their current roles by promises of spearheading exciting new scientific breakthroughs.



"The days of pricing drugs and devices independent of their clinical value are over. Life sciences companies are now challenged to define and measure that value, or they risk losing their pricing power to innovators and to those with superb clinical outcomes."

Dr. David Friend, Chief Transformation Officer in The BDO Center for Healthcare Excellence & Innovation

What Happens When Value is the Coin of the Realm

Life sciences innovation and competition are both in the midst of disruptive revolutions driven by scientific discoveries, legislation, the unsustainable growth in healthcare spending and consumer empowerment via technology.

As this disruption continues within the healthcare system, it will be more important than ever to understand how these forces will impact the pricing of new health technologies, medicines and services.

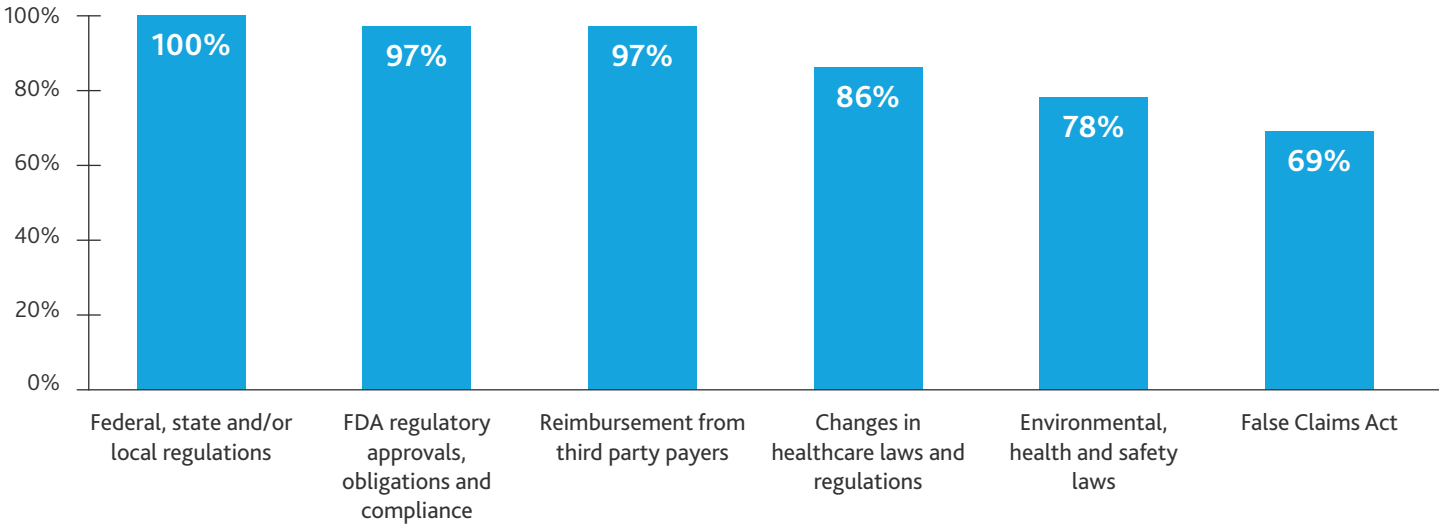
In the past, predicting pricing (and thus a business' cash flows) was relatively easy because there was no requirement to account for the "clinical value" of the product or service produced. The nascent move toward pricing new medications based on the value they bring to patients and society is one that every life sciences company, and its investors, must come to grips with. Slowly, but inevitably, value will become the coin of the realm, and life sciences companies must find new ways to define, measure and report on that value. New performance indicators are required, and new outlooks on what makes one drug or device better than another are being debated—is it the clinical effectiveness? Less disruptive, or even measurably positive, side effects? Ease of administering it to a sensitive population?

Defining these key performance indicators will be crucial to future pricing approaches. At the same time, society needs to balance the enormous investments required to produce these high-performing new drugs and medical technologies with the attendant risks and financial costs of research failure—a challenge compounded by a shift in who pays for treatment.

Consumers are becoming responsible for paying for a larger percentage of their drug costs out of their own wallets through a combination of increasing copayments, deductibles, tiered pricing arrangements and indication-specific pricing. We can expect consumers and those entities that negotiate for them, such as pharmacy benefit managers, health plans and consumer-focused e-commerce websites, to continue to revolutionize the purchasing process in the same way that consumer empowerment has revolutionized the travel industry, the retail industry and the transportation industry.

These pricing issues have made it more difficult for life sciences companies to forecast their earning potential. It's a challenge felt by companies at every stage in the life sciences business cycle, from startups seeking venture capital, to established companies managing the expectations of shareholders, to growing companies pursuing funding for new ventures, to those requiring up-to-date valuations to inform sales, mergers and other exit strategies. Those that are truly innovative and can prove their clinical value will command well-deserved premium pricing. Those that are not will either be made obsolete by others' innovation or they will find a stable price point that provides reasonable value for the clinical outcomes obtained.

REGULATORY CONCERNS HIGH AMID UNCERTAINTY



Regulatory Uncertainty Looms Large

Between the lengthy drug approval process, product labeling considerations and the ongoing impact of healthcare reform, the life sciences regulatory landscape is among the most complex. One hundred percent of life sciences companies analyzed report federal, state and local regulations as a risk to their business. There are a multitude of regulations that life sciences companies must abide by, including shifts in healthcare laws and regulations, cited by 86 percent of life sciences companies, up four percentage points from last year.

In an industry where product patents and exclusive marketing rights can shut competitors out for years, being first to market and continuous innovation are of the utmost importance—especially for companies that depend on a single product or a small number of products (cited as a risk by 54 percent of companies analyzed).

But developing a product is only half the battle; getting a drug or device through approvals to market presents its own hurdles and can determine a company's survival (particularly if that company is relying on a small number of products). Navigating the long road to U.S. Food & Drug Administration (FDA) approval is the industry's greatest regulatory challenge. According to Pharma.org, for every 5,000 to 10,000 experimental compounds considered, typically only one will gain FDA approval. Unsurprisingly, 97 percent cite FDA regulatory approvals and compliance as a risk. Ninety-one percent cite delays or unfavorable results from clinical trials, which can make or break the product at hand, particularly if it is in late stage development.

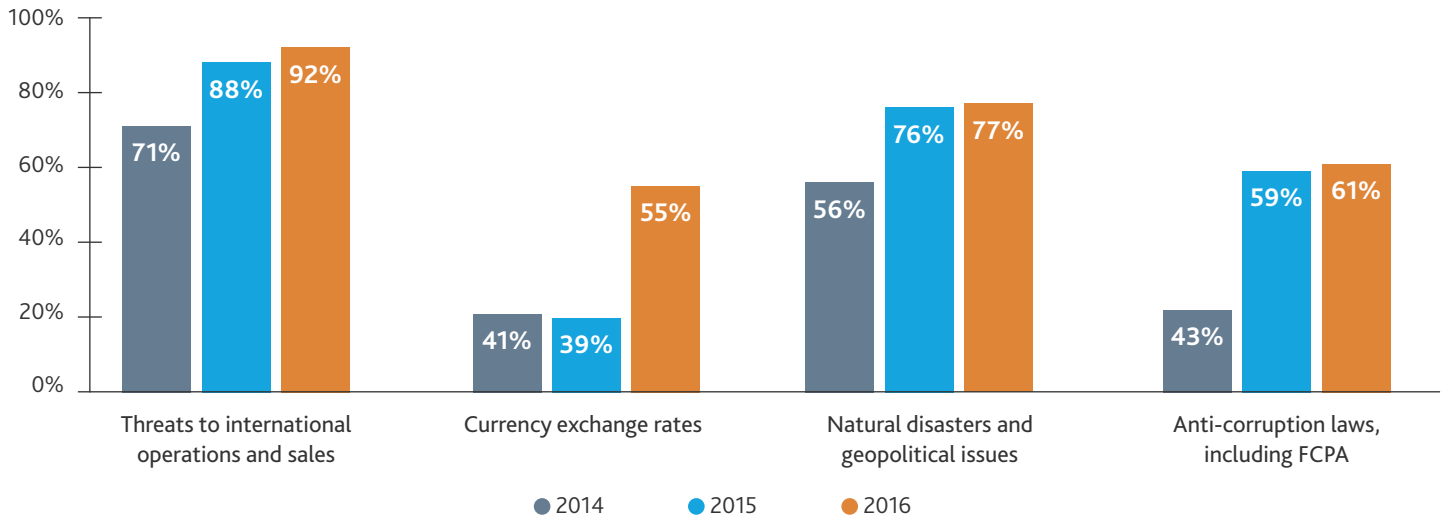
And while the ACA was relatively lenient on prescription drugs and medical devices, its changes to Medicaid and Medicare reimbursement and rebates have implications for life sciences companies. The Centers for Medicare & Medicaid Services finalized the ACA's Medicaid reforms for prescription medications in January, increasing rebates and setting upper limits on federal reimbursements, and shared a physician-administered drug payment reform model for prescription drugs under Medicare's Part B benefit in May. Continued uncertainty around the impact of new reimbursement models is causing a stir among life sciences companies in this year's analysis: 97 percent cite reimbursement from third party payers, including payments from Medicare and Medicaid, as a risk factor.

Additionally, over two-thirds (69 percent) of life sciences companies cite the False Claims Act (FCA) as a risk this year. Under the FCA, it is illegal to submit claims for payment to Medicare or Medicaid based on falsified or fraudulent information—and intent to defraud is not a requirement. The federal government recovered approximately $3.6 billion in settlements or judgments in FCA cases in 2015, with $1.9 billion of recoveries coming from healthcare-related FCA cases. The healthcare and life sciences industries are expected to see more FCA cases this year, driven by an increased focus on individual accountability and record-high awards to individual whistleblowers. The Supreme Court also unanimously issued a decision in June on the legal theory of "implied certification" that may expand FCA liability.

Collaborations Speed Up

Ninety-one percent of the largest U.S. life sciences companies cite risks related to collaborations in their annual filings. Partnering is a key strategy in the life sciences industry as both an engine of innovation and a source of financing. In the current financing environment, collaborations are an attractive option. Life sciences organizations continue to look to partner with entities developing innovative

RISKS RELATED TO GLOBAL OPERATIONS



technologies in order to bolster their development pipelines. Companies are also seeking collaborations with nontraditional partners like IBM and Google as healthcare and technology converge.

Life sciences companies are also leveraging M&A strategies to fill their pipelines. 2015 was a record-breaking year for deal activity, boasting 468 announced life sciences industry transactions, an 11 percent increase from 2014, according to the Thomson Reuters Deals Review. Despite a few notable megadeals in the sector, 2016 has gotten off to a slower start. The recently announced termination of the proposed $160 billion Pfizer-Allergan merger—and the new inversion rules behind its failure—may also have put a damper on activity and raises concerns about additional casualties. Three-quarters of companies cite the inability to manage, complete and integrate current or future transactions as a risk in their annual filings.

International Risks Mount, Even Pre-Brexit

The vast majority (92 percent) of life sciences companies cite threats to international operations and sales, up four percentage points from 2015, and 42 percent cite the ability to expand abroad in their annual filings. As companies grow their business overseas—particularly in emerging markets—they must grapple with different business conduct rules, regulations and cultural norms, increasing their risk of exposure to bribery and corruption. These inconsistencies from market to market create confusion over what constitutes a bribe, resulting in both accidental and purposeful misconduct. Sixty-one percent cite risk related to the Foreign Corrupt Practices Act (FCPA) and other anti-bribery regulations.

Under the FCPA, U.S. regulators have their eye on life sciences, probing some of the largest multinational pharmaceutical companies for international bribery violations. The DOJ recently announced a new one-year FCPA pilot program, encouraging broader civil enforcement and raising the threshold on what constitutes cooperation credit, in addition to strengthening coordination with foreign counterparts. In the DOJ's own words, "This should send a powerful message that FCPA violations that might have gone uncovered in the past are now more likely to come to light." The SEC and DOJ are also expanding their scrutiny of life sciences to include medical device and equipment manufacturers.

"In this environment, compliance can't be an afterthought; it needs to be viewed as a key business driver and an integral piece of strategy and risk management. Companies that establish a culture of compliance from the top down will be in the best position to mitigate risk. Without active participation and leadership from management as well as the board, compliance programs won't permeate the DNA of the organization and violations may occur."

Glenn Pomerantz, BDO Global Forensics Practice Leader, in an article for Pharmaceutical Compliance Monitor

International Taxation Updates for Life Sciences Companies

The rapid growth of the life sciences sector over the last few years has come at the price of increased scrutiny from regulators seeking to ensure that the industry's gains are generating broader macroeconomic benefit.

Most recently, we saw the proposed $160 billion merger of pharma giants Allergan and Pfizer fall apart in the face of new Treasury rules aimed at discouraging so-called tax inversions—transactions that allow U.S. companies to move their base of operations to countries with more favorable tax regimes. With 92 percent of companies in this year's Life Sciences RiskFactor Report citing threats to international operations as a key business risk, what are some the latest tax reform efforts life sciences entities should keep in mind as they seek to manage their growth—and stay on the right side of U.S. tax law?

Anti-Inversion Guidance

In April 2016, the Treasury and IRS announced temporary regulations codifying rules initially introduced by notices issued in 2014 and 2015 intended to discourage inversions and other tax-avoidance transactions. In addition, the temporary regulations set forth new rules addressing issues the prior notices had not discussed, including:

1. Rules for identifying a foreign acquiring corporation when a domestic entity acquisition involves multiple steps;

2. Rules that disregard stock of the foreign acquiring corporation that is attributable to certain prior domestic entity acquisitions;

3. Post-inversion rules that require a controlled foreign corporation (CFC) to recognize all realized gain upon certain transfers of assets described in IRC Section 351, which shift the ownership of those assets to a related foreign person that is not a CFC; and

4. Rules clarifying the definition of group income for purposes of the substantial business activities test.

In effect, the rules seek to make it more difficult for U.S. companies to remove income from the U.S. for the purposes of changing their tax residency. Read BDO's International Tax Alert for more details about these new regulations and what they may mean for companies considering an international transaction.

Debt/Equity Classifications for U.S. Tax Purposes

In addition to the inversion-specific guidance, the Treasury and IRS published proposed regulations in April 2016 addressing the characterization of certain related party debt instruments. The proposed regulations under Code Section 385 would authorize the IRS to treat certain related-party interests in a corporation as indebtedness in part and stock in part for federal tax purposes, and establish threshold documentation requirements that must be satisfied in order for certain related-party interests in a corporation to be treated as indebtedness for federal tax purposes. Additionally, the proposed regulations would treat certain related-party interests as stock that otherwise would be treated as indebtedness for federal tax purposes. **In classifying related party instruments as debt, companies may seek to reduce their tax liability by taking advantage of interest deductions. However, converting those instruments to equity may introduce a broader range of tax consequences—for example, interest payments may instead be treated as dividend distributions.** Additional information on the new Section 385 rules can be found in BDO's International Tax Alert on this topic.

Corporations had until July 7, 2016, to share their feedback on the Treasury's guidance on these issues, and the government hopes to finalize the rules by Labor Day. With the regulations set to impact a broad range of transactions—not just inversions—we expect to see healthy debate in the months to come.

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