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Life Sciences Law & Industry Report™

Outlook 2012

Life sciences industry attorneys and biopharma executives on the *Life Sciences Law & Industry Report* editorial advisory board and other experts described their top issues for 2012. Some of those listed—biosimilars, personalized medicine, mergers and acquisitions, patent reform—also were in the 2011 list, while others—''pay for delay'' settlement agreements, China, and India—are new. But even those previously listed have a new sense of importance. Patent reform was passed in 2011 and will be implemented, as will the abbreviated pathway for biosimilars approval. And the effect of personalized medicine on the industry, while more gradual than was once anticipated, is expected to continue. There was the feeling among those asked to comment that 2012 would be an important year for life sciences law and industry, although not one without its challenges.

Patentability, Biosimilars Top Life Sciences Issues for 2012

For the life sciences industry, 2012 will be a year when a lot of things are likely to come together, industry attorneys and executives told Bloomberg BNA during telephone interviews and e-mail exchanges in December.

They indicated that it could be a year when clarity about what is patentable subject matter is achieved from at least one and perhaps two Supreme Court rulings and when personalized medicine, which cuts across federal agencies, the private sector, and a number of other life sciences issues, could definitely become the focus of the industry. And it could be a year when implementing the abbreviated biosimilars approval pathway will result in stronger collaborations among biotechnology, pharmaceutical, and generic drug companies.

But the year also poses challenges to the life sciences industry with the America Invents Act (AIA), also known as the patent reform law, and a changing market model. There also are calls for the Food and Drug Administration to increase the speed of drug approvals; more effectively address social media issues, especially as they relate to the off-label use of drugs; and help alleviate drug shortage problems.

1. Patentable Subject Matter to Be Clarified. The prominent issue for those contacted by Bloomberg BNA is the potential clarification of what is patentable by the Supreme Court's upcoming ruling in *Mayo Collaborative Services v. Prometheus*, which will focus on the extent to which medical diagnostic methods are patent-eligible subject matter under 35 U.S.C. § 101 (5 LSLR 1238, 12/16/11). Another relevant case, if the Supreme Court grants certiorari, would be its ruling in *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, also known as the *Myriad* case, which addresses whether ''isolated'' DNA molecules constitute patentable subject matter (5 LSLR 1200, 12/16/11).

Howard W. Bremer of the Wisconsin Alumni Research Foundation, Madison, Wis., said, ''The decision in *Prometheus* could have a very substantial effect upon the potential validity of many outstanding patents as well as applications in the growing field of personalized medicine. What will be the relative role of 35 U.S.C. § 101 versus patentability issues under Sections 102 and 103 which focus on invalidity and obviousness? If the decision under Section 101 is that claims to methods for diagnosis and treatment are patent eligible, such claims

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may raise further considerations on associated joint, contributory, induced, and indirect infringement.''

Ronald M. Daignault of Robins, Kaplan, Miller & Ciresi's Life Sciences Group told Bloomberg BNA, ''Somewhat surprisingly, oral argument of the *Prometheus* appeal focused on the question of whether the patentability doctrines of novelty and obviousness are strong enough to prevent the issuance of patents from the U.S. Patent and Trademark Office that would stifle innovation in the diagnosis of human disease. It will be interesting to see whether the court provides specific instruction to the Patent Office and to the lower federal courts about the level of scrutiny that patents directed to medical diagnosis and treatment deserve.''

Rochelle K. Seide of RKS Consulting, Boca Raton, Fla., said, ''Based on the oral arguments, it appears that the diagnostic claims at issue in the *Prometheus* patent will be deemed to constitute patentable subject matter because they are sufficiently 'transformable' under the *Bilski* decision and the cases following it.''

As for *Myriad*, Seide said that it is not going away—yet. ''As I predicted in this space last year, the Federal Circuit found Myriad's patents directed to 'isolated' DNA molecules constituted patentable subject matter, even though most of their diagnostic method claims (using the patentable DNA molecules) were found to not constitute patentable subject matter, although that will be addressed in *Prometheus*.''

Philip T. Chase of Adimab LLC, Lebanon, N.H., indicated that the predictions for whether the Supreme Court will take the *Myriad* case, and if so, what it will do with it, range widely. ''Whatever they do, and particularly if they find Myriad's patents invalid, it will likely have significant ripple effects on the industry,'' Chase said.

Kevin E. Noonan of McDonnell, Boehnen, Hulbert & Berghoff LLP, Chicago, said these two cases and others have raised an issue that could extend beyond the Supreme Court's rulings, which is whether the ability to protect biotechnology inventions by patenting will continue.

It is possible that the Supreme Court will reverse 30 years of patent protection for a technology whose successes have relied upon patenting.

KEVIN NOONAN, MCDONNELL, BOEHNEN, HULBERT & BERGHOFF

''The frequent involvement of the Supreme Court in patenting matters, and its particular generalist perspective on patenting issues, raises the possibility that the court will reverse thirty years of patent protection for a technology whose successes have relied upon patenting,'' Noonan said. ''The consequences could be severe, ranging from a breakdown in the partnership between university research and businesses capable of commercializing the fruits of that research, to a tendency towards protecting 'second generation' biotech inventions by trade secret.''

Noonan added, ''This tendency will be exacerbated by provisions of the AIA that remove some of the disincentives against reliance on trade secrets.''

2. Biosimilars Act Implementation to Start. Sarah Rouse Janosik of Katten Muchin Rosenman LLP, Los Angeles, said that the landscape for biosimilars will continue to take shape in 2012. The Food and Drug Administration recently began formally implementing the Biologics Price Competition and Innovation Act of 2009 (4 LSLR 323, 4/9/10), which establishes an abbreviated FDA approval pathway for biosimilars, by announcing the proposal it will send to Congress to implement user fees for biosimilars (5 LSLR 1224, 12/16/11).

''Because there are currently no biosimilars approved,'' Janosik said, ''the FDA expects to expend significant resources up-front in evaluating research and protocols for biosimilar applications. FDA proposals in 2012 are expected to include those on generic names of biosimilars, clinical trial requirements and ability to rely upon foreign approvals, implementation of the 'interchangeability' provision, and characterization of molecules.''

Noonan suggested that whether biosimilars become viable will depend on whether FDA actually promulgates a regulatory biosimilars pathway.

''And even if the agency does provide clear guidelines, it remains a question of whether the economics will provide sufficient impetus for a company to risk the complicated litigation provisions to risk using the pathway,'' Noonan said. He added, ''It also is a question whether traditional generic drug companies will enter this area, or whether they will be outcompeted by traditional innovator companies, and whether these efforts will promote new discovery by funding it or inhibit it by taking resources from new drug development.''

Seide acknowledged that biosimilars is still a complicated topic even though the legislation was enacted more than a year ago and FDA has yet to issue its regulations on how it will implement the law. ''Despite this, more and more pharma and other companies (read Samsung) (5 LSLR 1210, 12/16/11) are indicating that they will enter the fray for developing follow-on biologics or biosimilars,'' Seide said. ''The thorny issues that could remain are the 'patent dance' in the law and how the innovator and follow-on filer can prepare for that and whether to seek approval by an alternate route such as the new Biologics License Application.''

Judith A. Hasko of Latham & Watkins LLP, Menlo Park, Calif., told Bloomberg BNA that during the last quarter of 2011, major collaborations for biosimilar product development were announced between biotechnology companies having larger-scale biologics development and manufacturing capabilities and pharmaceutical companies. ''The impending expiration of patents on blockbuster biologic products, combined with the new approval path for biosimilars, are driving these deals.''

Hasko stated that she expects to see similar collaborations between other biotech companies with relevant capabilities and pharmaceutical and/or generic drug companies in 2012 and possible acquisitions of biotechnology companies that have biologic development and manufacturing capabilities by companies wanting to establish a presence in biosimilars.

''Given that the law is so new, these deals will test and potentially inform the detailed implementation of this new legislation,'' Hasko said.

Attorneys for Robins, Kaplan, Miller & Ciresi's Life Sciences Group noted that the biotech giant Amgen Inc. and prolific generic manufacturer Watson Pharmaceu-

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ticals announced Dec. 19, 2011, a joint venture to produce biosimilar versions of several biologic medicines for cancer. ''It will be interesting to see what products, if any, emerge in 2012 from the combined experience of these two pharmaceutical powerhouses,'' they said.

3. FDA Will Face Many Challenges. Hasko said 2012 will be a year of challenge for the FDA, noting that in 2011 life sciences companies and investors expressed frustration with the positions FDA took in connection with therapeutic and medical device approval processes and standards (5 LSLR 1003, 10/21/11).

''Such commentators voiced their perception that the FDA's tough and possibly inconsistent approaches are confounding an already difficult product development environment. While in some respects these sentiments are not new, there is now a pervasive perception that FDA may be imposing unduly high hurdles to approval in some areas and circumstances. Such perception, if not addressed, will continue to amplify challenges life sciences companies face in a tough funding environment in 2012,'' Hasko said.

Chase noted that in 2011, the Biotechnology Industry Organization announced an effort to ''speed scientific breakthroughs, develop cures and grow the bioeconomy'' that included proposals that would allow for the speedier approval of drugs through a variety of mechanisms, including allowing FDA to use progressive approvals and a ''weight-of-the-evidence'' standard as opposed to a ''substantial evidence'' standard (5 LSLR 300, 3/25/11).

Chase said, ''BIO's initiatives echo several others, and there seems to be growing momentum behind rethinking the FDA approval process, especially as it applies to drugs for orphan diseases and deadly diseases for which there is currently no effective treatment, including for example, many cancers. If this momentum results in legislation—attached to the Prescription Drug Users Fee Act V, for example—we could see significant improvement in industry's ability to get drugs to patients more quickly and cost-effectively.''

Although the odds of the legislation passing are long, Chase said, ''This has become a significant public policy debate that should be getting more attention and an opportunity for us to really improve the way we develop new drugs.''

Janosik observed that the evolution of social media in the health care industry will continue in 2012 as patients' online presence grows and social media becomes part of health care organizations' overall strategies to enhance brand loyalty, to recruit new patients, and to improve services and outcomes. Others indicated that FDA seems to be struggling with how to deal with social media issues, especially as they relate to the off-label use of drugs.

Ian Spatz of Manatt Phelps & Phillips LLP, Washington, noted that on Dec. 27, 2011, FDA issued a draft guidance on the ability of regulated companies to respond to unsolicited requests for off-label information and said he thinks it will cause havoc in the industry.

''Although the draft acknowledges that companies have important information to contribute to online discussions of their products, the FDA has signaled that it will give companies little leeway in engaging in those discussions,'' Spatz said. ''When a company sees an off-label discussion, it may not provide correcting, additional, or any other information other than a general statement that the discussion contains information on an off-label use and information on where people may go within the company for additional information.''

In following this guidance, ''companies may not share truthful information generally with those who were exposed to the original information,'' Spatz said. ''This is a problematic—although not necessarily unexpected—omen concerning future FDA regulation of social media. We can expect more guidance on social media regulation from the FDA this year.''

Carol A. Pratt of K&L Gates, Portland, Ore.. agreed with Spatz that FDA's off-label guidance will pose a ''huge problem for the life sciences industry.'' She said that off-label promotion has been a high enforcement priority for the last decade but that ''the new arena for 2012 is expanding the battleground to the world of social media.''

''FDA is struggling with how its rules can deal with this new world, and its guidance shows it,'' Pratt said. ''Even say you're giving a presentation at a conference and someone asks a question about off-label use of a product. This happens all the time. You have a First Amendment right to answer the question, but FDA considers this situation off-label promotion. Its guidance says that you have to take this public situation and drive it into a private situation, have the person ask you in private because you cannot answer it in public.''

Pratt said FDA's draft guidance ''is not a very helpful map of how industry can deal with situations such as conference and online queries. It doesn't get FDA there. I believe it will be a significant issue that will play out over the coming months, maybe even in litigation.''

Personalized medicine ''is shaping life sciences. It will have a huge impact for the FDA, requiring it to prioritize a new framework for regulatory science.''

CAROL A. PRATT, K&L GATES

Janosik added that in 2012, FDA, along with health care providers and pharmaceutical manufacturers, likely will address supply-chain, inventory-tracking, and quality-control issues to combat the drug shortages that are the result of increased demand, manufacturing and quality deficiencies, discontinued products, and regulatory conflicts and that have delayed clinical trials and resulted in unprecedented price gouging as well as the increasing presence of counterfeit and gray market products.

4. Impact of Patent Reform. Janosik said that in 2012, life sciences professionals will face the ramifications of implementing the America Invents Act (5 LSLR 923, 9/23/11). ''Although President Obama and the U.S. Patent and Trademark Office have emphasized the positive impact that reform is expected to have on innovation, several provisions of the AIA could create major issues for biotech and life science companies,'' Janosik said.

Noonan said the AIA ''changes the dynamic involved in protecting biotech and life sciences inventions. These inventions typically take a long time to develop from an

initial discovery, typically in the university context. The emphasis on 'first inventor to file' and the inability to swear behind earlier disclosure should put pressure on university scientists who exist in the 'publish or perish' environment. While it is unlikely that companies will be able to prevent this type of disclosure, it may reduce the value of university patents, since the ultimate 'invention' may be so downstream of the initial discovery that there will be little value (and less licensing revenue) in this early discovery work.''

Bremer made special note of the AIA's post-grant review provisions and said that members of the information technology industry have submitted comments to the PTO to adopt procedural rules that define relatively low thresholds for the initiation of post-issuance review, define the terms ''real party interest'' and ''privy'' to limit the non-party estoppel effect of such review, and provide for relatively broad discovery and participatory rights to match those offered in the litigation context.

''Are these suggestions, if adopted, fair to all of the users of the patent systems even though available to them?'' he asked. ''It would seem that they would tend to favor larger entities over independent inventors, small businesses, and universities' technology transfer efforts where much less discretionary money is available and lead back to unlimited discovery and delays where prompt disposition should be the goal.''

5. Personalized Medicine—the New Direction? This issue has frequently been in Bloomberg BNA's top 10 list, but some of those contacted said that 2012 would be the year when personalized medicine would really begin taking hold.

Pratt found that personalized medicine represents a horizontal cross-cutting across a number of federal agencies and the private sector. ''It is shaping life sciences,'' Pratt says. ''It will have a huge impact for the FDA, requiring it to prioritize a new framework for regulatory science.''

Pratt said she could see a shift in interest toward the way medical devices are developed, in the industry, FDA, and in her own practice. ''Mom and pop companies don't do drug development, but you see these small companies doing a lot of innovation in medical devices.''

She said she could see the shift toward personalized medicine reflected in the work of in vitro diagnostic entrepreneurs and in FDA's sudden interest in laboratory developed tests. ''In in vitro entrepreneurial companies you see the type of business development that is the foundation of personalized medicine. And the private sector's development of novel diagnostic tests that have become a fast-track to market has FDA taking notice and indicating that they should be regulating them. The whole sector is bubbling up,'' Pratt said.

Personalized medicine has ramifications for Medicare coverage, Pratt said, since it advocates putting diagnostic tests at the front end. It also will have implications for intellectual property issues in 2012, the year after the AIA was passed. ''If personalized medicine is the health care of tomorrow, investors today need to know that there is certainty for their investment. IP issues are indeed different this year,'' Pratt said.

Hasko predicted that diagnostics would continue to gain momentum in 2012.

''In the past we've predicted a rapid increase in development of new diagnostics and predictive medicine products, but what we have seen has been a more gradual yet steadily increasing pace of development of these products, which will continue through 2012. These products will continue to attract more interest and investment given their relatively short development cycles and wider utility, with companies focusing on development of novel, high value-added diagnostics and predictive medicine products,'' Hasko said. ''We will continue to see more transactions addressing development of companion diagnostic products alone or in conjunction with therapeutic products.''

6. China, India, and Europe. Daignault said it will be important to watch China and India in 2012, noting that Ranbaxy Laboratories received approval Nov. 1, 2011, from Indian regulatory authorities to begin manufacturing and selling a new antimalarial drug—the first time an Indian drug company developed and brought to market a new chemical entity. ''This is a significant achievement and foretells future pioneering work that will come from Indian pharmaceutical and biotechnology research,'' Daignault said.

For the past several years, both China and India have deepened their commitment to life sciences research and development, Daignault said, with more and more industry conferences and scientific symposia being held in China and India every year and scientists and investors from around the world attending and paying close attention.

''The advancements that are being made in China and India will continue in 2012 and become more significant.''

RONALD M. DAIGNAULT, ROBINS, KAPLAN, MILLER & CIRESI

''The advancements that are being made in China and India will continue in 2012 and become more significant,'' Daignault said.

J. Mark Waxman and Stephen A. Bent of Foley & Lardner, Boston, saw reason for concern about the ''bubble'' mentality in Big Pharma with respect to the China drug market. ''This could represent more and more investment with little or no evidence of reasonable return on investment, and this could create a significant investment dynamic that may result in an additional element in favor of a 'pull back' in this sector,'' they said.

Noonan said that the effects of the European Court of Justice's ruling that human embryonic stem cells and methods using such cells are not eligible for patenting in Europe ''because they are against public morality'' also needs to be watched (5 LSLR 994, 10/21/11).

''This creates the possibility that investment and stem cell research will migrate from Europe to more hospitable climes, much like the human embryonic stem cell ban imposed by the Bush Administration caused a reduction of hESC research in the United States. It also remains to be seen whether individual countries in Europe will, like certain U.S. States, provide funding and protection outside the scope of the European Patent Office,'' Noonan said.

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7. M&As, the 'Patent Cliff,' and the New Pharma Model. Hasko told Bloomberg BNA that because the life sciences initial public offering market has been limited, in 2012, investors in private life sciences companies will continue to position their portfolio companies to attract potential acquirers. A portion of these acquisitions will continue to involve earn-out payment structures for companies with early stage assets, making investors' return dependent on future product-related milestones being achieved by the acquiring company.

Chase said the massive consolidation and layoffs in pharma over the last several years have created turmoil with big pharma and big biotech.

''Many of the largest pharma companies are still figuring out how they want to approach research and innovation,'' Chase said. ''Will they internalize their research or outsource it to biotech? Will pharma continue to focus on later stage assets or invest in novel technology? Will pharma have any appetite for doing innovation deals or will the trend continue toward biosimilars and generics and other 'safer' bets? As a result of this uncertainty, much of biotech is in limbo, and it will be fascinating to see how 2012 unfolds on the biotech partnering front.''

Waxman and Bent said, ''A perfect storm-like convergence of 'patent cliff' drug patent expirations, declining R&D productivity, and the wholesale retreat of venture funding from biotech will result in great pressure in the M&A and business-to-business collaboration arenas—see, for example, Gilead's $11 billion bid for Pharmasset (5 LSLR 1169, 12/2/11). How this will spread, in particular to pushing more investment or 'roll ups' in the medical device arena, remains to be seen.''

Noonan said that because many conventional small molecule drugs are coming off patent in the next few years and company revenues are expected to fall, large pharmaceutical companies' capacity to take advantage of start-up and university innovation to replenish their pipelines may be inhibited by less money for investment.

''Although it is an unlikely development, large pharmaceutical companies, or profitable companies with less conventional presence in the life sciences sector such as General Electric or Philips which sell MRI machines, for example, may have the opportunity to enter the area by funding startup companies with promising new technologies.''

Daignault said that advances in stem cell biotechnology will generate useful platforms for drug discovery that will pique the interest of the pharmaceutical industry.

''Recently, the U.S. government set aside $140 million to fund research projects to develop so-called 'human-on-a-chip' models—microscopic systems and miniaturized organs that can connect in realistic ways to simulate human body function,'' Daignault said. ''With this funding, researchers at the University of Central Florida, for example, recently announced a stem cell-based technique for growing a neuromuscular junction between human muscle cells and human spinal cord cells. This connection is critical for communication between the brain and muscles and will be useful for testing compounds that could modulate neuromuscular function and be useful in treating motor diseases like myasthenia gravis, amytrophic lateral sclerosis or spinal cord injury.''

8. Essential Health Benefits and ACOs. Wendy L. Krasner of Manatt Phelps & Phillips LLP, Washington, said that a recent effort to define and quantify essential health benefits (EHBs) poses major risks for life sciences companies in terms of future coverage of services and products, meriting immediate and focused attention.

Krasner told Bloomberg BNA that Dec. 16, 2011, the Center for Consumer Information and Insurance Oversight, which is part of the Centers for Medicare & Medicaid Services, issued an ''Essential Health Benefits Bulletin'' to provide information for states as they seek to certify health plans that will offer insurance coverage through state health insurance exchanges as of 2014.

''The CCIIO proposes a 'benchmark' approach to the scope of the required EHB package based on current offerings in the state, while offering a fair amount of flexibility to the states. While prescription drugs is one of the coverage categories that must be reflected in the benchmark, the language on drug coverage in the bulletin is problematic, as it appears to signal a formulary standard that is less comprehensive than the current Medicare Part D standard, specifically noting that one drug per category or class would be sufficient while the Medicare standard is two drugs,'' Krasner said.

The bulletin also could be read to create an invitation to state governments to limit drug coverage and redirect the savings into other services/products, Krasner said. ''The effort to define and quantify EHBs poses major risks for life sciences companies in terms of future coverage of services and products and is an arena that merits immediate and focused attention. Comments on the bulletin are due Jan. 31, 2012.''

Krasner also noted that, under what some view as the flagship provisions in the Patient Protection and Affordable Care Act, the CMS Innovation Center announced Dec. 19, 2011, the names of 32 leading health care organizations that will participate starting in 2012 in a new Pioneer Accountable Care Organizations (ACOs) initiative. Under the program, Medicare will reward groups of health care providers that have formed ACOs based on how well they are able to both improve the health of their Medicare patients and lower their health care costs. CMS also is in the process of approving somewhat less ambitious ACO arrangements under the Medicare Shared Savings Program.

''There has been a lot of attention paid to both types of ACOs, as well as others under development for state Medicaid programs and the commercial market, as a key focus of bridging the gap between fee-for-service reimbursement and traditional managed care capitation. It will be several years before it is known if these initiatives can contribute to a more efficient, better quality system,'' Krasner said. ''That said, however, the question will increasingly be whether the value of the medical technology as proposed by the life sciences industry supports the performance targets incentivized under these new value-based purchasing arrangements.''

Krasner said that life sciences companies ''should no longer be standing on the sidelines and watching ACOs evolve; rather, they need to understand these developments and have a plan as to how they will participate in this new reimbursement and coverage construct.''

9. 'Pay for Delay' Settlement Agreements. Attorneys for Robins, Kaplan, Miller & Ciresi's Life Sciences Group told Bloomberg BNA that Congress and the Federal Trade Commission seem more interested than ever in scrutinizing or even outlawing ''pay for delay'' pharmaceutical patent litigation settlements to make generic pharmaceuticals available to consumers more quickly and to reduce health care expenses relating to prescription drugs.

''The Preserve Access to Affordable Generics Act, currently pending in the 112th Congress, received a shot in the arm this fall from FTC and Congressional Budget Office studies claiming that several billion dollars in savings could be realized if such reverse payment settlements were declared illegal,'' the attorneys said. ''While election year politics may slow the legislative push, it is almost certain that antitrust challenges to these settlements in the courts will continue.''

Related to the issue of ''pay for delay'' settlements and the pending legislation is the way in which Pfizer responded to the launch of generic Lipitor. The Robins attorneys noted that Pfizer made various deals with pharmacy benefit managers and insurers, and undercut generic pricing to curb the loss of its Lipitor market share. Arguments have been made that Pfizer's tactics undermine the incentives for generic manufacturers to develop and market their products.

''The same criticisms have been leveled against outlawing pay-for-delay settlements,'' the attorneys said. ''As life sciences companies prepare themselves for biosimilars and follow-on biologics, close attention will be given to the way branded and generic companies act in the pharmaceutical drug market.''

10. Early Stage Funding Will Still Be Hard to Secure. For all the promise of many of the issues listed so far, Hasko reminded Bloomberg BNA that certain venture capital firms historically focused on life sciences investments could not raise targeted amounts for their new funds in 2011.

''Other venture capital firms that invest in an array of technologies are perceiving nearer term and greater returns outside of life sciences and are de-emphasizing life sciences investments. The formerly traditional model of venture capital funding of companies developing early stage life sciences technologies and then exiting through IPO is becoming a rarity,'' Hasko said.

''In 2012, we should see more innovative types of project-based funding begin to fill this early stage product development funding gap, but for many promising life science companies developing early stage products, this innovation may not arrive soon enough,'' Hasko concluded.

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