

No. 10-1150

IN THE
Supreme Court of the United States

MAYO COLLABORATIVE SERVICES
(D/B/A MAYO MEDICAL LABORATORIES)
AND MAYO CLINIC ROCHESTER,
Petitioners,

v.

PROMETHEUS LABORATORIES, INC.,
Respondent.

ON WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

**BRIEF FOR AMICI CURIAE
ROCHE MOLECULAR SYSTEMS, INC., VENTANA
MEDICAL SYSTEMS, INC., HOFFMANN-LA ROCHE
INC., AND ABBOTT LABORATORIES, INC.
IN SUPPORT OF NEITHER PARTY**

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INTEREST OF AMICI CURIAE¹

Amici curiae are leading biopharmaceutical companies and pioneers in the new clinical frontiers of molecular diagnostics and personalized medicine. As both

¹ No counsel for a party authored this brief in whole or in part, and no persons or entities, other than amici or their counsel, made a monetary contribution to the preparation or submission of this brief. Letters from the parties consenting to the filing of this brief are on file with the Clerk.

purchasers and sellers of patented diagnostic technologies, *amici* have a uniquely balanced perspective on the issues of public policy raised in this case.

Roche Molecular Systems, Inc., Ventana Medical Systems, Inc., and Hoffmann-La Roche Inc. are affiliates of F. Hoffmann-La Roche Ltd (collectively “Roche”), the world’s largest biopharmaceutical company. Close cooperation within Roche’s pharmaceutical and diagnostic divisions enable it to tailor treatments to specific patient subpopulations based on the latest scientific understanding of biology and disease at the molecular level. Roche develops and manufactures a wide array of innovative diagnostic products used in the diagnosis, prognosis, and treatment of cancer and infectious diseases. Some of Roche’s diagnostic tests utilize the company’s Nobel Prize-winning polymerase chain reaction (“PCR”) technology to detect the genetic material (DNA or RNA) in cancerous cells and infecting pathogens, such as HIV or hepatitis. Because the tests are capable of identifying and characterizing disease earlier and more specifically than tests based on the body’s immune response, patients can be treated and monitored with great precision. Roche’s tissue-based diagnostic tests enable the detection of genetic biomarkers that facilitate the ability of health care providers to prognose or even predict patient outcomes for various cancer therapeutic regimens. Roche has a broad line of oncology, virology, microbiology and blood screening tests, which are used by researchers, physicians, patients, hospitals, laboratories and blood banks around the world.

Abbott Laboratories, Inc. (“Abbott”) is a diverse, global health care company with scientific expertise and products that address the full range of health care needs—from disease prevention and diagnosis to treatment and cure. For more than 120 years, Abbott has

been a pioneer in developing innovative solutions that improve health and the practice of health care. Among other things, Abbott develops and markets tests that can detect subtle but key changes in patients' genes and chromosomes. These award-winning technologies permit earlier detection and diagnosis of diseases; assist in the selection of therapies that are more likely to prove effective; and improve the monitoring of disease progression. Abbott offers more than 350 products related to molecular diagnostics for infectious disease, oncology, genetics and automation, including breakthrough DNA probe technologies critical to the diagnosis and treatment of lung, breast, and bladder cancer.

Roche and Abbott invest billions of dollars annually in the research and development of diagnostic products and technologies. Patent protection is not merely critical to prevent free-riding on their substantial investments. It is necessary to provide appropriate incentives to invest in research, development, and innovation in areas like personalized medicine that hold the greatest promise for improving treatment and decreasing the costs of therapy for those suffering from often fatal diseases. The question presented in this case is therefore of great significance to both Roche and Abbott.

SUMMARY OF ARGUMENT

Patent protection is critical to the development of personalized medicine, which promises not only to improve patient health dramatically but also to curb the costs of providing safe and effective treatments. Denying patents for novel and nonobvious diagnostic tests ill-serves the Patent Act's purposes and Congress's goals in establishing the limits of patent eligibility under 35 U.S.C. § 101.

I. Personalized medicine is a new and revolutionary field that promises dramatic improvements in how we diagnose and treat disease. Rather than treat all cases of a particular disease identically, personalized medicine seeks to tailor diagnosis and treatment to each patient's unique genomic or molecular profile. The essence of personalized medicine is the use of diagnostic tests to identify certain biological traits or "biomarkers" that are associated with particular disease characteristics. For example, patients with a particular "biomarker" may respond to a specific treatment, whereas those lacking that marker will not. Identification of those biomarkers thus can form the basis for diagnostic or therapeutic decision-making. Government regulators, academics, and industry stakeholders have all recognized that the widespread adoption of personalized medicine promises to transform health care by improving patient care and reducing the costs associated with unnecessary or ineffective treatment.

II. Patent protection is essential to realizing the promise of personalized medicine. The discovery and validation of clinically useful biomarkers requires expensive and risky clinical trials, much like those in the biotechnology and pharmaceutical industries. Translating those discoveries into commercially viable diagnostic tests further requires demonstrating to regulators and insurers the clinical utility and cost-effectiveness of those tests. Given the significant investment and substantial risk entailed in the discovery, development, implementation, and regulatory approval of diagnostic tests, the incentives afforded by the patent system are critical to ensuring the growth of the personalized medicine industry in the United States.

III. The criticisms of patents for diagnostic tests are theoretical and unsupported by empirical evidence.

Patents in this field do not stifle innovation or frustrate the practice of medicine. The limited period of exclusivity afforded by patents provides the necessary incentives for prospective research, development, and commercialization of diagnostic tests, which greatly serve the long-term public interest. In the personalized medicine industry, as in the biopharmaceutical industry generally, market-driven business practices and self-enforcing market norms correct for any perceived limitations on the accessibility of patented diagnostic technologies. In any event, Congress has already spoken on the issue by exempting certain researchers and medical practitioners from liability for patent infringement. To the extent additional protections prove desirable, Congress retains the ability to refine the existing exemptions based on sound evidence and with due regard to the reliance interest of existing patent holders.

ARGUMENT

I. PERSONALIZED MEDICINE IS A NASCENT FIELD THAT PROMISES TO REVOLUTIONIZE THE HEALTH CARE INDUSTRY

A. Testing And Analysis Of Molecular Biomarkers Allows Doctors To Customize Disease Prevention, Diagnosis, And Treatment

Physicians, clinicians, and researchers have long recognized that people with the same disease often respond very differently to the same treatment. Traditional medicine relies on a trial-and-error approach to that problem. On average, less than half of patients respond positively to prescription medications; for the remainder, the drug is either ineffective or toxic. Spear et al., *Clinical Application of Pharmacogenetics*, 7 Trends Molecular Med. 201, 201-202 (2001); see also Phillips et al., *Potential Role of Pharmacogenomics in*

Reducing Adverse Drug Reactions: A Systematic Review, 286 J. Am. Med. Ass'n 2270, 2270 (2001) (adverse drug reactions are among the leading causes of death in the United States). As a result, scarce resources are wasted on the purchase of medicines that either do no good or actually harm the patient. Worse still, effective treatments are not implemented unless and until they are identified through a wasteful and potentially painful trial-and-error process.

Personalized medicine provides substantial progress in this regard by identifying, in advance, the treatments that will and will not likely work. Defined as the science and practice of customizing the prevention, diagnosis and treatment of disease based on molecular “biomarkers,” such as gene sequence variations, gene or protein expression levels, or metabolites, personalized medicine represents one of the most promising new clinical frontiers. See Personalized Medicine Coalition, *The Case for Personalized Medicine 2-4* (2009), available at http://www.personalizedmedicinecoalition.org/sites/default/files/TheCaseforPersonalizedMedicine_5_5_09.pdf (“*The Case for Personalized Medicine*”).²

At its core, personalized medicine involves the use of diagnostic tests to obtain information about molecular biomarkers that are correlated with particular disease characteristics. *The Case for Personalized Medicine* 4. If the test results show that a patient possesses particular biomarkers, that information can be used for

² Others define “personalized health care” and “personalized medicine” in different, often broader terms. See, e.g., PricewaterhouseCoopers LLP, *The New Science of Personalized Medicine: Translating the Promise into Practice* 3, 8 (Oct. 2009).

purposes of diagnosis, prognosis, predicting the future risk of disease, or selecting treatment regimens that are particularly suited to that patient. *Id.* at 4-7. For example, a particular biomarker may indicate the early presence of a particular disease, permitting effective treatment before symptoms even appear. Another may indicate that certain treatments will work most effectively, signaling that others can be safely disregarded as ineffectual or potentially harmful. *See infra* Section I.B. (providing specific examples).

Personalized medicine thus has the potential to decrease the incidence of adverse drug reactions dramatically. Physicians and clinicians are guided by custom-designed genetic or molecular tests that permit superior diagnostic and therapeutic decision-making. *The Case for Personalized Medicine* 4-5. Health care costs decline as well. Insurers are not saddled with the costs of needless tests and/or treatment regimens that later prove to be unnecessary at best. *Id.* at 6-7. Most importantly, patients receive an early diagnosis, followed by highly individualized treatment that maximizes efficacy while minimizing the potential for side effects and adverse reactions. *Id.* at 4-6.

B. Personalized Medicine Is A Rapidly Developing Field In Which Industry Participation And Collaboration Is On The Rise

As leaders in this field, *amici* have developed diagnostic tests and associated treatments that promise to save lives, prevent needless suffering, and save billions of health care dollars. Roche, for example, has designed a microarray device called the Ampchip® CYP450, which provides comprehensive detection of gene variations—including deletions and duplications—for the CYP2D6 and CYP2C19 genes. The Am-

pliChip® test assists physicians in determining the best therapeutic strategy and treatment dose for an estimated 25% of all prescription drugs, including many common psychiatric drugs (antipsychotics and antidepressants). Abbott's Urovysion Bladder Cancer test identifies genetic aberrations in urine specimens from persons with hematuria (blood in urine), allowing the early detection of bladder cancer before any morphological changes manifest, which can dramatically increase survival rates. Other biopharmaceutical companies have developed diagnostic tests that permit more accurate prognoses. Genomic Health, Inc., for example, markets the OncoType DX®, which predicts the likelihood of breast cancer recurrence and patient survival within 10 years of diagnosis. *See, e.g.,* Hornberger et al., *Economic Analysis of Targeting Chemotherapy Using a 21-Gene RT-PCR Assay in Lymph-Node-Negative, Estrogen-Receptor-Positive, Early-Stage Breast Cancer*, 11 *Am. J. Managed Care* 313 (2005).

The promise of innovations in this area is also reflected in new AIDS detection techniques. For example, the new fourth-generation Architect® HIV Ag/Ab Combo detects infections 7 to 20 days earlier than prior HIV antibody tests. It was the first FDA-approved test for the diagnosis of HIV-1 and -2 infections in pregnant women and children under two. Early detection of AIDS is obviously critical not merely to its treatment, but also to preventing its spread.

One area of personalized medicine that has garnered significant interest in recent years is “companion diagnostics,” which are a special class of diagnostic tests used to identify the patients most likely to benefit from a particular drug. *See* Food and Drug Administration (“FDA”), *Draft Guidance for Industry and Food and Drug Administration Staff—In Vitro Com-*

panion Diagnostic Devices 6-7 (July 14, 2011) (“FDA, *Draft Guidance*”) (defining companion diagnostic as a “diagnostic device that provides information that is essential for the safe and effective use of a corresponding therapeutic product.”).

Roche recently received FDA approval to commercialize its cobas® 4800 BRAF V600 Mutation Test, a diagnostic test that identifies patients who would benefit from the Roche drug Zelboraf®, which is indicated for the treatment of certain types of inoperable or metastatic melanoma.³ The FDA has also recently approved a new molecular diagnostic test—Abbott’s Vysis ALK Break Apart FISH Probe—for detecting rearrangements of the anaplastic lymphoma kinase (ALK) gene in non-small-cell lung cancer (NSCLC). That test identifies a genetic variation (the ALK fusion gene) that indicates a high likelihood that a patient will respond positively to Pfizer’s XALKORI® (crizotinib) therapy. These breakthroughs in the advancement of personalized medicine—and companion diagnostics specifically—permit cancer treatments that are custom-tailored to patients’ unique genetic profiles. By excluding patients who would not benefit from particular treatment, the companion diagnostics developed by

³ Zelboraf® and its companion diagnostic were cited by the FDA as a “great example of how companion diagnostics can be developed and used to ensure patients are exposed to highly effective, more personalized therapies in a safe manner.” Press Release, FDA, *FDA Approves Zelboraf and Companion Diagnostic Test for Late-Stage Skin Cancer* (Aug. 17, 2011), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm268241.htm>.

Roche, Abbott, and others in the industry also save health care dollars and prevent needless suffering.⁴

The development and commercialization of these diagnostic tests, and companion diagnostics in particular, is often a collaborative process that entails sharing of clinical samples, data, and other information among various industry participants. For example, Roche and Abbott together made one of the first significant advances in this area, leveraging the power of a companion diagnostic in connection with Herceptin® (trastuzumab). See PricewaterhouseCoopers LLP, *The New Science of Personalized Medicine: Translating the Promise into Practice* 7 (Oct. 2009). Herceptin® is a drug developed by Roche's affiliate Genentech, Inc., to treat a particularly aggressive form of breast cancer. Although only a small portion of those suffering from breast cancer will benefit from Herceptin®, for that subpopulation the drug is extraordinarily effective, increasing survival periods by an average of 25%. It is also highly effective in lowering the risk that early-stage breast cancer will return. *Id.*

Because of personalized medicine, Herceptin® treatment can now be targeted to the subset of the population for whom it has that life-saving and life-extending potential. Abbott developed and commercialized the first diagnostic test to identify those patients who exhibit over-expression of a protein known as human epidermal growth factor receptor type 2 ("HER-2") due to a genetic anomaly. That overexpression of the HER-2 protein is associated with certain particularly aggressive cancers.

⁴ Other examples of life-saving companion and molecular diagnostics abound. A more comprehensive list may be found in *The Case for Personalized Medicine* at 18.

Most importantly, it also predicts whether the patient will have a dramatic response to treatment with Herceptin®. Thus, HER-2 companion diagnostics not only identify patients who will respond to Herceptin®, it also helps identify patients who will not, avoiding the costs and life-threatening delays associated with unnecessary Herceptin® treatment. See Hillner & Smith, *Do the Large Benefits Justify the Large Costs of Adjuvant Breast Cancer Trastuzumab?*, 25 *J. Clinical Oncology* 611, 612 (2007); see generally Dendukuri et al., *Testing for HER2-positive Breast Cancer: A Systematic Review and Cost-Effectiveness Analysis*, 176 *Can. Med. Ass'n J.* 1429 (2007). More recently, the FDA approved Roche's new tissue-based genetic test for the measurement of HER-2 in breast tumor tissue, which uses standard light microscopy. Unlike prior fluorescence diagnostics, Roche's new light microscopy-based HER-2 test can be performed in a standard laboratory, improving the accessibility of HER-2 testing for patients worldwide.

The development of companion diagnostics for Herceptin® illustrates the success of personalized medicine and the promise it holds for the future of the health care industry. Herceptin® and its companion diagnostic tests for HER-2 have had a major impact in the treatment of cancer, including metastatic breast cancer. See Tan & Swain, *Ongoing Adjuvant Trials with Trastuzumab in Breast Cancer*, 30 *Seminars in Oncology* 54, 54 (2002). Absent the promise of patent protection, there would be little incentive for biopharmaceutical companies to develop and market either an initial diagnostic test or improved, next-generation methods of detecting such potentially fatal diseases.

C. Personalized Medicine Is Expected To Have A Significant Impact On The Future Of Health Care In The United States

Personalized medicine has become a priority health care issue at the highest levels of government. Following a wide-ranging review of the field, the President's Council of Advisors on Science and Technology concluded that "personalized medicine warrants significant public and private sector action to realize the development and introduction into clinical practice of this promising class of new medical products." President's Council of Advisors on Science and Technology, *Priorities for Personalized Medicine 1* (Sept. 2008) ("*Priorities for Personalized Medicine*"). The current Director of the National Institutes of Health ("NIH") has observed that "personalized medicine remains one of the most compelling opportunities we have to improve the odds of staying healthy." Collins, *Personalized Medicine: A New Approach to Staying Well*, Boston Globe, July 17, 2005, at E12.

Congress and the Executive Branch have begun laying the foundation for investment in research and infrastructure necessary to support a rapid expansion in personalized medicine over the coming decades. In 2006, the Department of Health & Human Services ("HHS") launched the "Personalized Health Care Initiative" for the purpose of coordinating "activities in HHS agencies that could help accelerate a personalized health care future." HHS, *Personalized Health Care: Pioneers, Partnerships, Progress 13* (2008) ("HHS, *Personalized Health Care*"). One of the key priorities of the FDA is to "stimulate innovation in clinical evaluations and personalized medicine to improve product development and patient outcomes." FDA, *Advancing Regulatory Science at FDA: A Strategic Plan 10-13* (Aug. 2011). This past

year, NIH and FDA announced “a new collaboration on regulatory and translational science to accelerate the translation of research into medical products and therapies ... to help make personalized medicine a reality.” Hamburg & Collins, *The Path to Personalized Medicine*, 363 *New Eng. J. Med.* 301, 304 (2010).

Congress recently enacted legislation that calls for improvements in health care services through comparisons of the effectiveness of various treatments in patient subpopulations. *See* Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 3011, 3013, 3113, 6301, 124 Stat. 119, 378-79, 381-82, 422, 727-28 (2010).⁵ Such initiatives are intended to set the stage for further research and development activities that will increase the number of diseases and treatments for which commercial diagnostic tests are available. Garber & Tunis, *Does Comparative-Effectiveness Research Threaten Personalized Medicine?*, 360 *New Eng. J. Med.* 1925, 1925 (2009).

II. PATENTS ARE CRUCIAL TO PROVIDING PROPER INCENTIVES TO INVEST IN PERSONALIZED MEDICINE AND RELATED ADVANCES

A. Commercialization Of A Diagnostic Test Requires Substantial Investment In Research And Development

The biotechnology industry relies heavily on patent protection to encourage the investments necessary to convert inventions that might otherwise exist only on

⁵ Personalized medicine was also the subject of earlier congressional efforts at health care reform. *See, e.g.*, Genomics and Personalized Medicine Act of 2007, S. 976, 110th Cong. (2007); Genomics and Personalized Medicine Act of 2008, H.R. 6498, 110th Cong. (2008).

paper into commercially viable products that improve the health and quality of life of the public. Many of these inventions are based on clinical data that lead to the correlation of one or more biomarkers with disease prognosis or predictive response to a therapeutic—the heart of personalized medicine.

In 2011, publicly-traded companies in the United States alone invested more than \$22 billion in biotechnology-related research and development. Ernst & Young, *Beyond Borders: Global Biotechnology Report* 37-39 (2011). The average cost of bringing a single biotechnology-related therapeutic to market, including basic research, clinical trials, and post-approval testing, exceeds \$1.2 billion. Grabowski, *Follow-On Biologics*, 7 *Nature Reviews Drug Discovery* 479, 482 (2008). For every successful product, many more are abandoned, often only after substantial investments that cannot be recouped. *Id.* at 481 (only 30% of biological therapeutics that make it as far as human trials succeed); see generally Graham et al., *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 24 *Berkeley Tech. L.J.* 1258, 1277, 1288, 1290 (2009) (finding that patents are considered important to innovation in the biotechnology and medical device sectors). Investments in this area can be justified only if the returns on successful products are sufficient to cover the costs of developing not merely those products but also the many more that end in failure.

Much like in the biotechnology industry generally, the research and development activities needed to make advances in personalized medicine are extremely costly. To make a molecular biomarker such as a genetic sequence clinically useful, the first task is to find associations between the biomarker and a disease or

drug response. “Such studies usually require thousands of participants and the collection and preservation of a large number of biological specimens and genetic material, and as such can go well beyond the resources of a single company or laboratory.” *The Case for Personalized Medicine* 9. Once the association has been discovered, clinical trials are required to demonstrate and validate the clinical utility of the association. Many such trials are equivalent to pharmaceutical trials in both design and scope, sometimes involving following patients for years to determine long-term safety and efficacy. *See generally* HHS, *Personalized Health Care* 83. Bringing a single diagnostic product to market typically requires tens of millions of dollars and can cost well over \$100 million under certain circumstances, an investment coupled with several years of research and clinical studies involving hundreds of patients. *See, e.g., id.* at 84-85.⁶

Finding the private capital needed to fund the clinical research required to discover and validate a broader array of biomarkers is one of the greatest challenges facing the personalized medicine industry. *See* HHS, *Personalized Health Care* 83. Diagnostic products generally offer a very low rate of return on investment, particularly in light of the staggering amounts required for their development. *Id.* at 83-85; *see generally* Kling, *Diagnosis or Drug? Will Pharmaceutical Companies or Diagnostics Manufacturers Earn More from Personalized Medicine?*, 8 EMBO Rep. 903 (2007).

⁶ In 2009, biopharmaceutical companies spent over \$5 billion in research and development activities directed towards companion diagnostics. *Id.* at 85-86. Roche and Abbott spend more than \$1 billion annually on developing diagnostic products and systems.

Even apart from the costs and risks involved in this area, private investors are often deterred by greater demands from regulators and insurance providers for clinical evidence demonstrating safety and effectiveness. Human Genetics Comm'n, *Intellectual Property and DNA Diagnostics: A Report of a Seminar on the Impact of DNA Patents on Diagnostic Innovation* 5-6 (Oct. 2010) ("*Intellectual Property and DNA Diagnostics*"). The FDA, for example, is increasingly requiring that diagnostic products satisfy the same clinical and pre-market criteria as those usually reserved for pharmaceuticals and medical devices. See FDA, *Draft Guidance* 8-10; Press Release, FDA, *FDA To Host Public Meeting on Oversight of Laboratory-Developed Tests* (June 16, 2010), available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm215766.htm?sms_ss=twitter. Most insurers, including the Centers for Medicare & Medicaid Services, do not ordinarily reimburse the costs of diagnostic screening tools, and certain predictive tests are not reimbursed at all. See *The Case for Personalized Medicine* 12; HHS, *Personalized Health Care* 88. As in the biotechnology and pharmaceutical industries, there is simply no guarantee *ex ante* that investments in research and development will be recouped through a commercially viable product. See, e.g., *Intellectual Property and DNA Diagnostics* 5-6; *Personalized Health Care* 85.

B. Patents On Diagnostic Tests Are Necessary To Promote Innovation And Clinical Research

In light of the costs and high risk of failure, patents are critical to promising investors the realistic possibility of a reasonable financial return from those diagnostic products that actually make it to market and pre-

venting others from simply free-riding on the discoveries they have funded. In a 2008 report on the subject, the President's Council of Advisors on Science and Technology concluded that

The ability to obtain strong intellectual property protection through patents has been, and will continue to be, essential for pharmaceutical and biotechnology companies to make the large, high-risk R&D investments required to develop novel medical products, including genomics-based molecular diagnostics.

Priorities for Personalized Medicine 21.⁷

Indeed, there appears to be a broad consensus among regulators, industry participants, and legal commentators that patent protections are vital to creating proper incentives for clinical research in the area of personalized medicine. See Nat'l Research Council, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* 20, 25 (Merrill & Mazza eds., 2006) ("Nat'l Research Council, *Reaping the Benefits*") ("intellectual property protection is essential to ... enable firms to garner the sustained investments needed for diagnostic and drug development and testing"); Toneguzzo, *Impact of Gene Patents on the Development of Molecular Diagnostics*, 5 *Expert Op. Med. Diag.* 273,

⁷ In March 2000, investors mistakenly interpreted statements by President Clinton and British Prime Minister Blair as announcing their intention to narrow patent protection for gene-based innovations. Although the statements were later clarified, leading American biotechnology companies lost \$50 billion in aggregate shareholder value over the following two weeks. Davies, *Cracking the Genome* 205-207 (2001).

275 (2011) (“For validation of molecular diagnostics, patents are critical to incentivize the significant investment required for these activities.”); Paci et al., *Impact of DNA Patents on Pharmacogenomics Research and Development: Economic and Policy Issues*, 71 *Drug Dev. Res.* 485, 490 (2010) (patent protections “can stimulate private investments in an underexploited field with great potential for innovation and public health”); Sung, *Alarming Challenges Facing Medical Technology Innovation*, 6 *J. Bus. & Tech. L.* 35, 55-56 (2011) (“Tinkering with patent eligibility ... may bring unforeseeable consequences, including the unfortunate chilling of future innovation.”).⁸

For their part, Roche and Abbott filed about 350 priority patent applications in 2010 in an effort to protect their diagnostics research and development, while also timely sharing their scientific advances with the public. Roche and Abbott firmly believe that patenting their advancements is critical to their ability to continue their investments and forward planning in the diagnostic arena. See, e.g., F. Hoffmann-La Roche Ltd, *Genes & Health* 45, 116 (2007), available at http://www.roche.com/genes_and_health.pdf.

⁸ Some commentators argue that patents are not necessary because the costs of researching, developing, and commercializing diagnostic tests are lower than those in the biopharmaceutical industry generally. See, e.g., Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, 9 *Nw. J. Tech. & Intell. Prop.* 377, 389-394 (2011); Sec’y’s Advisory Comm. on Genetics, Health, & Soc’y, Dep’t of Health & Human Servs., *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 30-35 (2010). That minority view rests on the premise that FDA and insurance providers will not subject diagnostic tests to the same level of scrutiny as pharmaceuticals and medical devices. As noted in Section II.A. above, that assumption has proven incorrect.

A ruling that novel and nonobvious diagnostic tests are ineligible for patent protection would cripple the nascent personalized medicine industry. Two decades of effort directed toward optimizing the delivery of health care through personalized medicine would be lost. Small companies and start-ups would be particularly devastated because they rely on regular infusions of capital from investors, who often insist on the availability of patent protection as a precondition to funding ongoing research and development efforts. *See, e.g.*, Biotechnology Industry Organization, *Guide to Biotechnology* 2, 77 (2008); Barfield & Calfee, *Biotechnology and the Patent System* 27 (2007); Grabowski et al., *The Market for Follow-On Biologics*, 25 Health Aff. 1291, 1299 (2006).

III. PATENT CLAIMS DIRECTED TO DIAGNOSTIC TESTS NEITHER HARM PATIENTS NOR IMPEDE THE PROGRESS OF SCIENCE

A. Patents On Diagnostic Tests Do Not Pose An Obstacle To Scientific Research

Petitioners and their amici argued below that patents on diagnostic tests stifle innovation and basic scientific research. This claim is largely based on speculation, rather than sound evidence. *See* Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 Nature Biotech. 1091 (2006). The long-standing “conventional view” is precisely to the contrary: biomedical research “is more likely to be impeded by lack of access to privately held research inputs such as materials, data and know-how than by patents.” Chandrasekharan et al., *Proprietary Science, Open Science and the Role of Patent Disclosure: The Case of Zinc-Finger Proteins*, 27 Nature Biotech. 140, 140 (2009).

In fact, “empirical research suggests that the fears of widespread anticommons effects that block the use of upstream discoveries have largely not materialized.” Caulfield et al., 24 *Nature Biotech.* at 1093; *see also* Adelman & DeAngelis, *Patent Metrics*, 85 *Tex. L. Rev.* 1677, 1681 (2007) (“The existing empirical studies find few clear signs that the patenting of biotechnology inventions is adversely affecting biomedical innovation.”); Paci, 71 *Drug Dev. Res.* at 485 (“recent evidence on genetic testing suggests that many of the issues might have been overestimated or overemphasized”). The Federal Trade Commission (“FTC”) likewise noted that “concern previously centered on the belief that biotechnology patent protection was too strong” and “would actually obstruct commercialization of new products, thereby hindering follow-on innovation. This problem has yet to materialize.” FTC, *Emerging Health Care Issues* 32 (2009) (footnote omitted).⁹

For example, in the area of molecular diagnostics, “the evidence shows that patents do not inhibit research leading to new discoveries and, in fact, may in some cases stimulate it through the disclosure of inno-

⁹ A 2005 survey of scientists involved in biomedical research found that “patenting does not seem to limit research activity significantly, particularly among those doing basic research.” Walsh et al., *Patents, Material Transfers and Access to Research Inputs in Biomedical Research* 3 (Sept. 20, 2005) (“Walsh, *Patents & Access*”); *see also* Walsh et al., *View From the Bench*, 309 *Science* 2002 (2005). An earlier study found that patents “rarely precluded the pursuit of worthwhile projects.” Walsh et al., *Working Through the Patent Problem*, 299 *Science* 1021, 1021 (2003) (“Walsh, *Working Through the Patent Problem*”). When requested, licenses were often available at minimal or no cost. Walsh, *Patents & Access* 17. “Thus, not only are barriers or delays rare, but costs of access for research purposes are negligible.” *Id.*

vations.” Toneguzzo, 5 Expert Op. Med. Diag. at 275; *see generally* Caulfield, *Human Gene Patents: Proof of Problems?* 84 Chi.-Kent L. Rev. 133, 135-139 (2009) (reviewing numerous studies and finding no evidence of constraints on research). The key barriers to the widespread adoption of personalized medicine are not the existence of patents, but the lack of clear regulatory guidelines for approval of molecular diagnostics and the failure of insurers to provide standardized coverage criteria for diagnostic testing. Toneguzzo, 5 Expert Op. Med. Diag. at 275.

B. Patents Do Not Impede Patient Access To Diagnostic Tests

Petitioners and their amici argue that patents preclude meaningful patient access to diagnostic testing, frustrate the practice of medicine, and ultimately disserve the public interest. Those are precisely the types of concerns that Congress considered and rejected in broadly defining the classes of patent-eligible subject matter. *See, e.g., Eli Lilly & Co. v. Premo Pharm. Labs., Inc.*, 630 F.2d 120, 138 (3d Cir. 1980) (“Congress has determined that it is better for the nation in the long-run to afford the inventors of novel, useful, and nonobvious products short-term monopolies on such products[.]”).

Once an invention has been discovered and the manner of its operation disclosed to the world, it is facile to argue that the public would be better off if the invention were not patented. That ignores the critical antecedent question: would that invention exist if it were unpatentable? In the area of diagnostics, and personalized molecular diagnostics in particular, the answer is often “no.” Absent patent protection, there would be little or no incentive for diagnostics compa-

nies to complete any existing projects, disclose discovered correlations between biomarkers and health-related traits, or bring any additional products to market. Sacrificing incentives for patient access runs the serious risk that patients may not have anything to access.

In any event, the evidence adduced by the petitioners and their amici is, at best, inconclusive. *See* Caulfield, 84 Chi.-Kent L. Rev. at 139-141 (concluding that “the studies available are relatively few in number and of limited methodological strength”). Patents appear to have little, if any, monopolistic effect on the price of diagnostic tests. *See* Cook-Deegan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 Genetics Med. S15, S23-24 (2010). And it is well known that market exclusivity through patent protection creates strong incentives for advertising efforts that educate patients and health professionals who are interested in purchasing the end product. *See generally* Donohue et al., *A Decade of Direct-to-Consumer Advertising of Prescription Drugs*, 357 New Eng. J. Med. 673, 680 (2007). As with pharmaceuticals and medical devices generally, the incentive to inform the public about patented diagnostic products creates a social benefit by improving access and creating awareness among at-risk individuals. Cook-Deegan, 12 Genetics Med. at S32; *see also* Sorrell v. IMS Health Inc., 131 S. Ct. 2653, 2670 (2011) (describing the “benign and, many would say, beneficial speech of pharmaceutical marketing”).

To the extent there are any legitimate issues of patient access, those issues are best resolved through market-driven approaches, such as patent pools and

patent clearinghouses, rather than the blunt instrument of a blanket declaration of patent ineligibility. Stakeholders in the personalized medicine industry should be permitted to explore such collaborative licensing arrangements, which have succeeded in alleviating perceived barriers to entry and access in other industries. See Verbeure et al., *Patent Pools and Diagnostic Testing*, 24 Trends in Biotech. 115, 118 (2006); Ebersole et al., *Patent Pools as a Solution to the Licensing Problems of Diagnostic Genetics*, 17 Intell. Prop. & Tech. L.J. 1, 8 (2005); Toneguzzo, 5 Expert Op. Med. Diag. at 275.

C. “Rational Forbearance” Against Researchers And Medical Practitioners Is The Industry Norm

Petitioners and their amici have raised concerns of infringement suits against doctors and researchers and of patents directed to obvious common sense. *E.g.*, Pet. 29-30 (asserting that diagnostic patents “prevent medical researchers and providers from thinking about ... correlations in different ways”); AARP Cert. Br. 5 (hypothesizing patents on correlating “being a woman with an increased risk of becoming pregnant, and being elderly with an increased risk of suffering from Alzheimer’s disease”). These fears are as misplaced as they are hyperbolic.

Patent holders in the biopharmaceutical industry are generally loath to threaten enforcement against the scientific and medical communities. Pressman et al., *The Licensing of DNA Patents by Large U.S. Academic Institutions: An Empirical Survey*, 24 Nature Biotech. 31, 37 (2006); Mossinghoff, *Remedies Under Patents on Medical and Surgical Procedures*, 78 J. Pat. & Trade-mark Off. Soc’y 789, 796-797 (1996). “Rational forbear-

ance” from patent enforcement against non-commercial and/or non-competitive uses of patented technologies has become an industry norm that plays “a significant role in ensuring the broad use of many genomic technologies.” Fore Jr. et al., *The Effects of Business Practices, Licensing, and Intellectual Property on Development and Dissemination of the Polymerase Chain Reaction: Case Study*, 1 J. Biomed. Discovery & Collaboration 7, 16 (2006); see also Nat’l Research Council, *Reaping the Benefits* 121-122. Roche, for example, has a long-standing policy of licensing its patented diagnostic technologies at little or no cost for research purposes. Fore, 1 J. Biomed. Discovery & Collaboration at 10 (noting that Roche’s stance with respect to non-commercial use of diagnostic patents was “in line with the traditional corporate practice of ‘rational forbearance’”). Abbott similarly cooperates with researchers and innovators to support their important work.

Patent holders are reluctant to upset the norm of open access in the research and medical communities for fear of losing reciprocal privileges to materials and information. See Walsh, *Working Through the Patent Problem* 1021. Experimental and clinical uses are likely to benefit patent holders by increasing the value of patented technologies. Putative infringers in the academic and medical communities are, therefore, often viewed as prospective partners in the development of the technology. *Id.*; Pressman, 24 *Nature Biotech.* at 37.

Patent holders, moreover, have little or no incentive to pursue costly litigation or licensing efforts. In the context of non-commercial or non-competitive uses of patented technologies, the amount of damages at stake is not likely to justify incurring the risk of patent invalidation and the negative publicity associated with an infringement suit.

The biopharmaceutical industry thus has strong incentives not to impede research and medical uses of patented diagnostic technologies, but rather to continue the dissemination of patented diagnostic tools and methods. There is no reason to believe that diagnostic method patents will have a future effect that is any different from their effect in the past: encouraging investment in personalized medicine and other breakthrough techniques for the benefit of patients and health care generally without posing any significant burden on research. The Court should not rewrite the law of patent eligibility based on strongly-worded accusations that are not supported by the empirical evidence.

D. Concerns About The Impact On Basic Research And Patients Have Been, And Should Continue To Be, Addressed By Congress

Rather than amending section 101 to limit the scope of patent-eligible subject matter, Congress has enacted certain liability exceptions to address the very concerns raised by the petitioners and their amici. For instance, 35 U.S.C. § 271(e)(1) provides significant protections to researchers:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

In *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005), this Court held that this statutory research exception is broad enough to encompass even *commercial* research activities as to which there is a reasonable

basis to believe that the research will produce the types of information relevant to a regulatory filing. *Id.* at 206-208. Basic research for non-commercial purposes continues to be protected under the common law research exception. *See Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600) (Story, J.); *see also Madey v. Duke Univ.*, 307 F.3d 1351, 1355 n.3 (Fed. Cir. 2002); *Deuterium Corp. v. United States*, 19 Cl. Ct. 624, 632 n.14 (1990).

Similarly, arguments directed to perceived limitations on clinical use and patient access have little merit in light of 35 U.S.C. § 287(c)(1), which provides,

With respect to a medical practitioner's performance of a medical activity that constitutes an infringement under section 271(a) or (b) of this title, the provisions of sections 281, 283, 284, and 285 of this title shall not apply against the medical practitioner or against a related health care entity with respect to such medical activity.

That limitation on remedies was enacted specifically to address the concern that patents on medical methods could unduly restrict the practice of medicine and adversely affect public health. *See* H.R. Rep. No. 104-863, pt. 7, § 616 (1996); *see also* Mossinghoff, 78 J. Pat. & Trademark Off. Soc'y at 795 n.17. Notably, Congress did not extend the immunity to "the provision of ... clinical laboratory services," 35 U.S.C. § 287(c)(3), "the practice of a patented use of a composition of matter in violation of [a] patent," or "the practice of a process in violation of a biotechnology patent," *id.* § 287(c)(2)(A).

To the extent a different balance is to be struck, the prerogative lies with Congress. This Court should, as it has in the past, refrain from crafting judicial limitations on patent-eligible subject matter based on an-

ecdotal evidence. *See, e.g., Diamond v. Chakrabarty*, 447 U.S. 303, 316-317 (1980) (ignoring the “potential hazards in considering whether respondent’s invention is patentable subject matter”). The political branches are uniquely suited to making informed compromises based on empirical evidence and careful study of the competing interests in this emerging and complex industry. *Id.* at 317 (“The choice we are urged to make is a matter of high policy for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot.”).

CONCLUSION

For the foregoing reasons, Roche and Abbott respectfully submit that, in deciding the scope of patent-eligible subject matter under 35 U.S.C. § 101, the Court should consider the importance of patent protection in the personalized medicine industry and the serious adverse consequences of invalidating patents directed to the inventive features of diagnostic tests.

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