No. 15-1182

In The
Supreme Court of the United States

SEQUENOM, INC.,

Petitioner,

v.

ARIOSA DIAGNOSTICS, INC., NATERA, INC., and DNA DIAGNOSTICS CENTER, INC.,

Respondents.

On Petition For A Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit

BRIEF OF *AMICI CURIAE* AMARANTUS BIOSCIENCE HOLDINGS, INC., EXO INCUBATOR, INC., AND MICHAEL HELTZEN IN SUPPORT OF PETITIONER

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STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

Amicus Curiae Amarantus Bioscience Holdings, Inc. ("Amarantus") is a small entrepreneurial biotechnology company focused on commercializing new diagnostics and therapeutics. Through its diagnostics division, Amarantus is developing the LymPro Test®, which is a blood-based assay to diagnose Alzheimer's disease, and MSPrecise®, which is a proprietary, next-generation DNA-sequencing assay for identification of patients with relapsing-remitting multiple sclerosis.

Amarantus is also developing: a drug (Eltoprazine) to treat quality-of-life degrading symptoms associated with Parkinson's disease; an engineered skin to replace skin lost by burn victims who are burned on at least fifty percent of the surface area of their bodies; and a peptide therapeutic, MANF, currently indicated for the treatment of Retinitis Pigmentosa.

Amicus Curiae EXO Incubator, Inc., is a biotechnology incubator focusing on developing extracellular vesicle and exosome technologies. EXO Incubator uses

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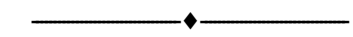
[1] Notice of the intention to file this brief was given to the parties at least ten days prior to the due date hereof. Counsel for all parties have consented to the filing of this brief, and their consents have been lodged with the Clerk of this Court. No counsel for any party had any role in authoring this brief, and no person other than the named *amici* and their counsel has made any monetary contribution to the preparation and submission of this brief. *See* Rule 37.

its intellectual property, start-up and business experience, resources, and industry networks to create unmatched competitive advantages for its partnered ventures. EXO Incubator brings a toolbox of resources and knowledge in the fields of genetics, genomics, transcriptomics, and proteomics, leveraging these technologies where they intersect with the emerging fields of extracellular vesicles and exosomes.

Amicus Curiae Michael Heltzen is a serial entrepreneur, business developer, and seed investor with over a decade of experience incubating, forming, and guiding new businesses. Mr. Heltzen has been a co-founder, board member, CEO, president, and vice president of various startups including BlueSEQ, CLC Bio, the Copenhagenomics Foundation, AllSeq Inc., and EXO Incubator.

Amici Curiae Michael Heltzen, EXO Incubator, and Amarantus have a strong interest in informing this Court of the deleterious and widespread effects arising from misapplication by judges and patent examiners of this Court's *Alice*/*Mayo* test. That misapplication results in indiscriminate invalidation of patent claims. Such invalidation, among other things, hinders bringing life-saving therapeutics and diagnostics to patients who stand to benefit from them. It also discourages innovation and harms U.S. economic competitiveness. To prevent lasting damage, this Court should grant certiorari and provide guidance concerning the proper application of the *Alice*/*Mayo* test.



ARGUMENT

I. The *Alice*/*Mayo* Test Has Been Misapplied; the Court's Guidance Concerning the Proper Application of the Test Is Needed

Amici are entrepreneurs that collectively have decades of experience starting, nurturing the growth of, and running new technology and biotech companies. Their experience tells them that a robust patent system is essential for entrepreneurs taking the high risk of developing revolutionary healthcare technologies or biotech businesses. For many such businesses, patents are the company's most important asset. A robust patent system is necessary because, without patent protection, companies cannot recoup the sizable investment of time and capital required to develop and commercialize their products. Furthermore, without patent protection, startups will not share their knowledge with partners, authorities, and peer-reviewers. The equation is simple: fewer protective patents means less funding of innovation, which leads to fewer new companies producing fewer new healthcare technologies and services, which ultimately results in diminished U.S. economic strength, increased healthcare spending, and prolonged patient suffering.

The patent system is not robust in the area of life sciences and healthcare innovation. Judges and the

USPTO are applying this Court's *Alice/Mayo*[2] test in a cursory way that facially invalidates any claim containing a judicial exception.[3] Cursory claim invalidation for failure to meet the historically low patent subject matter eligibility bar[4] has commercial and economic ramifications of which this Court – focused as it is on the law – is unlikely to be fully apprised. *Amici* present some of these ramifications so that this Court can more fully appreciate why its guidance concerning application of the *Alice/Mayo* test is now so sorely needed.

II. New Company Funding Is Drying Up Because Patents Are Being Indiscriminately Invalidated Under Section 101

Funding – which, along with the entrepreneur's time, is the lifeblood of new life science companies – is

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[2] *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014). Under the two-part *Alice/Mayo* test, a court must first ask "whether the claims at issue are *directed to* one of those patent-ineligible concepts"; if so, then the court must ask, "[w]hat else is there *in the claims* before us?" *Id.* at 2355 (citation omitted) (emphasis added).

[3] The "judicial exceptions" to patentability were explained in *Gottschalk v. Benson*, 409 U.S. 63 (1972), as follows: "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Id.* at 67. Since diagnostic methods involve observation and quantification of phenomena of nature, most diagnostic methods involve a judicial exception.

[4] 35 U.S.C. § 101.

injected into new companies by investors and large groups of entrepreneurs. But the *Alice/Mayo* test, as applied by judges and patent examiners, is causing new company funding to dry up. The reason is clear: the ability to obtain and successfully assert patents is a prerequisite to obtaining funding in life sciences and healthcare technologies, but application of the *Alice/Mayo* test calls this ability into question.

Amicus Michael Heltzen and his co-founders at EXO Incubator are focused on helping startups and groups of entrepreneurs develop and commercialize their ideas in the new field of exosome technology and biology. Cells in the body use exosomes, as humans use text messaging, to send short and precise messages to each other so that each cell knows what is occurring in other places in the body. Exosome technology and science, though complex, have potential to deliver precision medications only to those individual cells in the body that need the medications. Thus, they can change the conventional view of drugs from chemicals affecting all places in the treated body to ultra-precise treatments affecting only those cells in need of medication and thus lacking the side effects of drugs in use today. Exosome startups are significant because of their potential to cut down on adverse drug reactions – the fifth leading cause of death in the U.S.[5] And the foregoing are only a sample of the

[5] *Adverse Drug Reactions*, Public Citizen's Health Research Group (2016), available at http://www.worstpills.org/public/page.cfm?op_id=4 (last accessed April 12, 2016).

many positive possibilities emerging from the new ability to hear what human cells are saying to each other.

Amici have been told point-blank by investors and larger companies that partnering to develop complex but promising exosome technology will not occur because patents in this area cannot be trusted. In particular, larger companies – believing that judges' and examiners' misapplication of the *Alice*/*Mayo* test has made patents largely worthless – wonder why it makes sense to put a decade's worth of effort into a startup when someone else will just be able to come along and steal that co-developed technology.

Relatedly, *amicus* Amarantus believes that § 101 analyses are completely unpredictable – a veritable "wild west" – and that such uncertainty undercuts investment appetite for *in vitro* diagnostics.

All *amici* believe that such uncertainty undercuts desire for partnership and for undertaking the complex and risky work needed to advance new technologies beyond the prototype stage. The lack of trustworthy patents in this area makes entrepreneurs, startups, investors, and partners ask: Why should we take years' worth of risk and bear huge costs if, thereafter, anyone can come along, take the result of that collective effort, and sell it cheap because the taker never had to make any comparable investment of time or money?

III. Companies That Would Have Brought New Technologies to Market Are Not Being Formed Because of Indiscriminate Invalidation of Patents Under Section 101

Amici Michael Heltzen and EXO Incubator regularly counsel scientists who approach them about translating cutting-edge technologies and scientific ideas into practical, real-world applications. As such, these *amici* have developed proprietary models to determine whether or not to recommend starting a company on the basis of a particular cutting-edge technology.

Misapplication of the *Alice/Mayo* test by judges and patent examiners has caused a recalibration of these proprietary models. Based on current models, fifty percent or more of new companies that previously would have been formed do not get a formation green light from EXO Incubator's screening experts. The result is that half never get formed, and, because of the problems in the U.S. patent system, more of the approved companies are formed and headquartered overseas. Ironically, China has become *more* patent friendly than the U.S. Europe, too, has a relatively effective patent system. Other commentators have made similar observations about the relative abilities to get patents in the U.S. as compared to other jurisdictions, and the effects of this imbalance.[6]

[6] *See*, *e.g.*, Robert L. Stoll, *New patent subject-matter eligibility test hurts US competitiveness*, The Hill (2016), available at

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IV. U.S. Innovation Is Being Hurt, and U.S. Economic Competitiveness Is Being Damaged, Through Misapplication of the *Alice*/*Mayo* Test

An inability to fund and start new companies has national economic repercussions. When technologies are not commercialized, or cannot be adequately patent-protected, innovation is crushed. *Amici* are not alone in holding these hard-won views.

Robert Stoll, a former commissioner of patents at the USPTO, recently echoed these thoughts.[7] Going further, David Kappos, a former director of the USPTO, has "called for the abolition of Section 101 of

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http://thehill.com/blogs/pundits-blog/technology/267139-new-patent-subject-matter-eligibility-test-hurts-us (last accessed April 13, 2016) ("The *Mayo* test stands in contrast to the approach in Europe, where claims are analyzed to assure they have a technical character. If they do, they are evaluated as to novelty and inventive step. . . . Even in China, patents are granted as long as the claims contain a technical feature distinctive from the prior art. A patent claim in China will overcome the 'technical solution' hurdle if it uses a 'technical means.' This leads to broader patent subject-matter eligibility in China when compared to the U.S. American industry – particularly biotech and software – is already feeling the impact of an erosion in patent eligibility.").

[7] "From the perspective of those creating meaningful innovation like the examples outlined above, the European and the Chinese approaches to patentable subject matter are preferable to the current U.S. doctrine. Continued invalidation of large swaths of discovery and innovation domestically will result in a shift of jobs and economic growth to areas where innovators can take advantage of broader patent protection." *Id*.

the Patent Act, which sets limits on patent-eligible subject matter, saying decisions like *Alice* on the issue are a 'real mess' and threaten patent protection for key U.S. industries. . . . [Kappos said] that the U.S. Supreme Court's high-profile Section 101 decisions in *Mayo*, *Myriad* and *Alice*, *and the way lower courts have interpreted them*, have made it too difficult to secure patents on biotechnology and software inventions."[8] Kappos further noted that "patent officials in other nations have reacted with 'bemusement' as the U.S. invalidates patents on Section 101 grounds, while foreign companies that compete with American businesses see a golden opportunity in the reduced patent protection for software and biotechnology."[9]

It is no accident that there is a positive correlation between patent friendliness and economic competitiveness. As Mark Twain stated over a hundred years ago: "A country without a patent office and good patent laws is just a crab and can't travel any way but sideways and backwards."[10] If new companies cannot get enforceable patents with claims of commercially relevant scope,[11] new companies will not get funded and started.

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[8] Ryan Davis, *Kappos Calls For Abolition Of Section 101 Of Patent Act*, Law360 (April 12, 2016) (emphasis added).

[9] *Id*.

[10] Mark Twain, *A Connecticut Yankee in King Arthur's Court* (1889).

[11] Patent claims of commercially relevant scope strike a balance between scope of market protection and preemption.

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V. Misapplication of the *Alice*/*Mayo* Test Is Inappropriately Reallocating Resources and Human Capital

A basic management premise is that you get what you incentivize. At present, only one out of six National Institutes of Health ("NIH") grants is now being funded – down from one out of three NIH grants being funded a few years ago.[12] Consequently, academic scientists and their university employers look to new companies as a way to commercialize research and replace dwindling funding, *e.g.*, through licensing revenues and sale of appreciated founder's stock.

When a scientist or engineer invents a potentially life-changing technology that is not commercialized because of the current state of § 101 analysis, the ensuing disappointment has concrete repercussions.

Claims must be broad enough to provide a protection level that makes developing and marketing the invention commercially viable. On the other hand, as previously noted by this Court, the claims cannot result in total preemption of the "judicial exception" to patentability – *i.e.*, the abstract idea, natural phenomenon, or law of nature – present in the diagnostic method claims: "[Our precedents] warn us against upholding patents that claim processes that too broadly preempt the use of a natural law." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012).

[12] *See* Sen. Elizabeth Warren's remarks during the U.S. Senate's Health, Education, Labor and Pensions Committee hearing on *Achieving the Promise of Health Information Technology: Improving Care Through Patient Access to Their Records*, September 16, 2015.

Scientists and engineers who are blocked from commercializing a technology switch fields. These scientists and engineers – who are known collectively as "human capital" – are effectively reallocated. The technology spaces in which they work are also reallocated. Worse yet, this reallocation occurs not because it is in the best interests of society, and not because of the nature and usefulness of the ideas and technologies, but rather because of misapplication of the *Alice/Mayo* test by judges and patent examiners. Because the reallocation of human capital and resources is due not to the free market but rather to misapplication of the *Alice/Mayo* test, companies and innovators like *amici* urge this Court to issue corrective guidance to judges and examiners.

VI. Indiscriminate Invalidation of Patents Under Section 101 Harms Patients and Increases Healthcare Costs

The above-described reallocation that is due to misapplication of the *Alice/Mayo* test has real-life consequences for healthcare and for U.S. citizens. Resources are being shifted away from the development of: new diagnostic tests that can catch diseases earlier, when the diseases are easier to treat and have a better treatment prognosis; new live-saving drug types with fewer side effects; and new tissue-specific drug-delivery systems (that, for example, will replace toxic all-body chemotherapy). Thus, fewer of these innovations will be available to patients.

As a result, diseases will not be caught as early as they otherwise could. Rather, they will be treated later and with sub-optimally effective drugs that have higher costs and unwanted side effects. Patient lives will be shortened and made more painful. Productive citizens will be permanently lost to the workforce and their families because of disease-related disabilities and deaths. All these outcomes are personally and economically costly.[13]

VII. This Court Should Grant Certiorari and Provide Guidance Concerning the Proper Application of the *Alice*/*Mayo* Test

The Court can and should provide guidance that corrects the misapplication of the *Alice*/*Mayo* test. The guidance proposed by *amici* is straightforward: instruct judges and patent examiners when determining patent subject matter eligibility to evaluate each claim *as a whole rather than evaluating each claim element in isolation*.[14] Such guidance can remedy the

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[13] *See*, *e.g.*, *The Effect of Health Care Cost Growth on the U.S. Economy*, Final Report for Task Order # HP-06-12 Prepared for the Office of the Assistant Secretary for Planning and Evaluation, United States Department of Health and Human Services, available at https://aspe.hhs.gov/sites/default/files/pdf/75441/report.pdf (last accessed April 10, 2016).

[14] As noted *supra* in note 2, the first step in the *Alice*/*Mayo* test asks "whether the claims at issue are *directed to* one of those patent-ineligible concepts." The first test step — by its plain wording — does not ask the question of whether the claims at issue merely *contain* one of those patent-ineligible concepts *(i.e.,* judicial exceptions). To determine what a claim is *directed*

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problems described above and is fully consistent with the plain wording of the *Alice/Mayo* test.[15]

CONCLUSION

Judges and examiners misapply the *Alice/Mayo* test by facially invalidating all claims that contain a judicial exception. Such misapplication is fatal to new companies, damages the U.S. economy, crushes innovation, inappropriately reallocates resources and human capital, harms patients, and increases healthcare costs. This Court can remedy these problems by granting certiorari and instructing that,

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to, a court or examiner must construe and evaluate the claim *as a whole*. Otherwise, the plain wording of the first *Alice/Mayo* step is not being followed. Even if the claim is directed to a judicial exception, then, under the second test prong, judges and examiners should examine the remaining claim elements to determine whether they reflect combinations or improvements that exist for the purpose of applying the judicial exception.

By contrast, under the *Alice/Mayo* test as currently applied, the claim *never* gets evaluated as a whole. First, judges and examiners ask whether the claim merely contains a judicial exception. Second, they evaluate the remaining claim elements (i) in isolation or (ii) collectively but without regard to their combined effect with the judicial exception.

[15] "The good patent gives the world something it did not truly have before, whereas the bad patent has the effect of trying to take away from the world something which it effectively already had." Giles Sutherland Rich, 1978 60 JPOS 271,288, cited in CIPA Guide to the Patents Act, page 83 and Gaster/Marlow, CRi 1/2009 pages 3-4.

when applying the *Alice*/*Mayo* test, judges and examiners should evaluate the claim as a whole and not individual claim elements in isolation.

Respectfully submitted,

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