Questions for Rick Brandon AAU
Questions from Senator Tillis

1. Would the proposed legislation enable the patenting of laws of nature?

The proposed legislation would not enable the patenting of laws of nature. First, any invention or discovery that is not a process, machine, manufacture, or composition would be excluded from patent protection without any further analysis being required. Any invention or discovery that falls into one of those categories would then have to meet the usefulness standard, which requires the invention or discovery to provide "specific and practical utility in any field of technology through human intervention."

We do not see how this leaves room for patenting of laws of nature, nor the patenting of natural phenomena, mental processes, or abstract intellectual concepts. This comports with the overwhelming majority of the testimony that the Subcommittee heard. We have not heard any specific examples of laws of nature that arguably could meet such language, but we would be willing to review examples if anyone has put them forward.

The proposal maintains the standard that specific, practical *applications of* laws of nature would be patent eligible, because almost every invention depends upon natural laws and their application. Courts frequently speak about the ineligibility for laws of nature (such as the Archimedes principle or E = mc2); however, in practice, inventors, rightfully, seek claims like the one in *Diamond v. Diehr*, where the Arrhenius equation was *applied* in a process to cure rubber.

2. Would the proposed legislation enable patenting of human genes?

We understand that Chairman Tillis and Ranking Member Coons' intention is not to allow the patenting of genes as they exist in the human body and perhaps also not to allow the patenting of isolated human genes. If our understanding is accurate – and even though we believe all human genes now to be in the prior art – we might suggest that the forthcoming legislative text clarify and make explicit the Senators' intention without creating too many strictures.

We note a potential disconnect in some of the dialogue on the proposed legislation. Chairman Tillis and Ranking Member Coons have stated that they do not intend to overrule that *Myriad* holding. (The *Myriad* court held: "We merely hold that genes and the information they encode are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material.") In response, there has been testimony and other public commentary supporting overruling of *Myriad* in order to promote research and development of treatments based on natural products. For example, Sherry Knowles published a long list of examples of important natural drugs that were developed under the pre-Mayo, pre-Myriad system (penicillin, Amoxil, tetracycline, cyclosporin, cephalosporin, streptomycin, chloramphenicol, Taxol,

doxorubicin, vincristine, vinblastine, and many others). In our view, it is important that inventors are able to patent the medical diagnosis of treatments based upon the innovative discovery of correlations, *so long as* the invention is innovative by meeting Sections 102 and 103. The limited holding of *Myriad* relates to genes (at least those that are not modified by a human), while the discussion relates to other natural products. We do believe that natural drugs should be patentable, because significant research and cost can be required to discover and develop them, and because the public will not benefit from them at all if they are not discovered and developed in the first place.

Ultimately, AAU believes that our system needs to have *Myriad* not stand for the proposition that all isolated and purified natural products fail to meet Section 101. For the reasons stated, such inventions should be patentable because we want such treatments available to the public, but only where they meet Sections 102, 103, and 112.

3. Will allowing more diagnostic patents prevent the discovery of novel treatments for diseases?

No, we do not believe that diagnostic patents prevent the discovery of novel treatments for diseases. Nor will the patenting of chemicals discovered from nature stifle research and innovation. To the contrary, patents (including on medical diagnostics) promote investment, commercial development, and progress.

If any concern has been expressed as to the freedom for U.S. researchers to operate within such as system, there are a variety of ways that research is protected from patent suits, such as the exemption under Section 271 and the Hatch-Waxman system. We did not see the stifling of research prior to *Mayo* and *Alice*. Myriad is a good example, since we believe there were more than 10,000 scientific research papers published on the BRCA genes between 1997 (when Myriad's patents issued) and 2013 (when the four claims were invalidated). Indeed, many natural drugs were developed under the pre-*Mayo*, pre-*Myriad* system.

American universities, companies, and research institutes have the resources and talent in place to do great things. But significant investment beyond those resources and talent are required to bring medical innovations to patients. And our daily experiences at our universities demonstrate that patents are typically essential to gaining the investment necessary to develop medical innovations. In short, patents make the discovery of novel treatments more – not less – likely to be researched and brought to the market.

4. Will allowing diagnostic patents prevent developing and improving diagnostic tests?

No. For the same reasons as to treatments of disease, allowing diagnostic patents will promote – not prevent – the development and improvement of diagnostic tests. Patents will motivate the discovery and development of medical diagnostics. As discussed, patenting also provides a disincentive to attempting to keep diagnostic correlations as trade secrets. Myriad is illustrative

on this point. Prior to the ACLU lawsuit, we understand that Myriad made public the advances in identifying disease-related variants as the number of women tested increased and the number of Variants of Unknown Significance declined. Once having been sued, Myriad seems to have stopped this practice. This has led to the situation where, today, it is possible that Myriad knows of variants that correlate with the likelihood a woman will develop breast or ovarian cancer, but the scientific community does not. This puts competitors at a disadvantage, scientifically and commercially, because the Myriad test is more comprehensive than its competitors (Myriad having a vast head start in the number of patients it has screened). The Mayo/Alice framework incentivizes this type of behavior, to the public's detriment.

5. Will the proposed legislation increase certainty, or decrease certainty?

The proposed legislation would greatly increase certainty, even without further discussion and refinement. The 2018 joint IPO/AIPLA proposal provides another suitable alternative that would greatly increase certainty (ineligibility "(a) if and only if the claimed invention as a whole (i) exists in nature independently of and prior to any human activity or (ii) is performed solely in the human mind."). More predictability is essential to our system. In *Alice* and its progeny, the Supreme Court judicially imposed a complicated and unworkable framework that requires looking for an inventive concept, often without analyzing specific prior art and with limited analysis. This insight into the effects of these Supreme Court decisions is supported by a number of judicial statements, such as Judge Alan Lourie and Judge Pauline Newman in *Berkheimer*, and Judge Lourie in *Ariosa*." Former Chief Judge Michel testified to this Subcommittee that he could not predict eligibility in any given case, saying, "If I can't do it, how can bankers, venture capitalists, business executives and all the other players in the system make reliable predictions and sensible decisions?" And although the PTO, through Director Iancu, has sharpened PTO guidance and examiner training, true correction can only occur through legislation that clearly defines for the courts what is patentable subject matter.

Our patent system cannot advance the purposes for which it was created without being able to clearly and predictably identify the types of inventions that are eligible for patent protection, prior to comparing the inventions to the prior art. While the proposed legislation would filter out subject matter according to the same legitimate basic principles under which we used to operate, it will more clearly define what types of inventions deserve a proper patentability analysis under Sections 102, 103, and 112.

6. Do the underpinnings of the Patent Clause apply to medical diagnostics and software?

Yes, the underpinnings of the Patent Clause definitely apply to medical diagnostics and software. As discussed in *Diamond v Chakrabarty*, the 1952 Act was intended to provide for a broad definition of patentable subject matter. ("The Committee Reports accompanying the 1952 Act inform us that Congress intended statutory subject matter to "include anything under the sun that is made by man." S Rep. No 1979, 82d Cong., 2d Sess., 5 (1952); H.R.Rep. No. 1979, 82d Cong., 2d Sess., 6 (1952).") The patent clause is based on Congress having the power to grant

patents that "promote progress . . . of the useful arts," i.e. inventions. The history of the patent system, including the recent history of implementation of the Bayh-Dole Act, has resulted in unprecedented progress over the past 30-40 years. This is precisely what the Founders intended the patent clause to do. Patents encourage innovation and development of products that benefit the public, and while conditions for different fields and products obviously differ, medical diagnostic and software inventions can (and often do) require significant investment, involve human ingenuity, and provide useful information that provide the basis for later inventions - just as many other types of inventions do. Promoting those significant investments through patents, subject of course to the limitations of patentability under Sections 102 and 103, will benefit the public and our economy.

7. What investment is required to make available a medical diagnostic?

Just like the question of whether a potential drug might be effective and safe, the work of discovery and development of medical diagnostics is very risky. Both require not only the original discovery of the drug or diagnostic correlation but also testing, distribution, and availability. See, for example Flier, J.S., "Academia and industry: allocating credit for discovery and development of new therapies," J Clin Invest. 2019;129(6):2172-2174. Significant investment, both in terms of time and capital, is often required to make a diagnostic available to patients. While situations vary, we know that it can take many years and tens of millions of dollars to make available a medical diagnostic. This is just one reason the *Ariosa* and *Cleveland Clinic* cases were disappointing to many. The tests involved in those cases were innovative and took significant time and resources to develop. Medical diagnostics ready for use with patients are not a commodity, even with the significant investment we make in research in the United States.

The stories of American diagnostic companies help to illustrate the investment required to make medical diagnostics available. Exact Sciences Corporation is a molecular diagnostics company in Madison, Wisconsin focused on early detection and prevention of some of the deadliest forms of cancer. As described in the attached statement, Exact Sciences invested tens of millions of dollars and years of time in order to bring to patients its Cologuard® non-invasive stool-based DNA screening test. Exact Sciences, which was started before 2010, was able to obtain financing and momentum for its Cologuard development prior to the Supreme Court and subsequent court decisions that negatively impacted the ability to obtain and enforce patents in the diagnostic field. Because of this (and based on the other comments in our testimony and comments), we believe that had Exact Sciences initiated its Cologuard program a few years later, the company may have had a much more challenging path to bring its test to patients and providers. Millions of people might not have benefitted as quickly from this non-invasive cancer screening technology, and thousands of new jobs might not have been created. And if that's the case, if this technology were ever developed later in time, it is possible that it could have emerged in or from regions outside of the United States that do allow for patenting of such technologies, as discussed in other testimony. The patent system affords inventors and investors

the opportunity to recoup investments of the magnitude that Exact Sciences describes, and without that opportunity, life-changing innovations like Cologuard may not be feasible.

8. Are you advocating for the patenting of abstract ideas or natural phenomena?

No, we are not advocating for the patenting of abstract ideas or natural phenomena, nor do we see that others are so advocating. As discussed in our response to Question 1, the proposed legislation would not allow for the patenting of laws of nature, natural phenomena, mental processes, or abstract intellectual concepts.

9. We want to be sure that whatever legislation we pass works within the context of patent law as a whole. How do you see 101 fitting together with other sections of the current law?

Section 101 was conceived to be, and should be, a general screen for eliminating types of inventions for which the patent system was not intended. As discussed in *Diamond v Chakrabarty*, the 1952 Act was intended to provide for a broad definition of patentable subject matter. ("The Committee Reports accompanying the 1952 Act inform us that Congress intended statutory subject matter to "include anything under the sun that is made by man." S Rep. No 1979, 82d Cong., 2d Sess., 5 (1952); H.R.Rep. No. 1979, 82d Cong., 2d Sess., 6 (1952).") Section 101 is not where one looks at the prior art, and it is not supposed to be the fix to trolling issues or the high expense of federal litigation. If an invention passes the test, then one moves on to analysis under Sections 102, 103, 112 analysis. This is both what was intended and what makes sense.

10. There's been a lot of talk in this debate about what shouldn't be patented, but I haven't heard anyone come out and say patenting itself is bad. Can you provide us an overview of what patent protections provide and how organizations like yours use them to benefit the public?

The U.S. patent system serves two primary purposes. First, patents incentivize the creation and development of breakthrough discoveries by granting a limited period of exclusivity for inventions and discoveries awarded patent protection that justify the expense of development. Second, the patent system encourages disclosure of breakthrough inventions and discoveries by requiring applicants to publicly describe their inventions and discoveries so that others may use them once the period of exclusivity expires. Each of these purposes facilitates the transfer of inventions and discoveries from university laboratories into products or services that improve the world. American universities perform a significant amount of research and, stimulated in large part by the Bayh-Dole Act, generate thousands of inventions and discoveries that could potentially improve lives, much of it being the result of fundamental research. While often the result of millions of dollars of research support, most university inventions and discoveries are still extremely early stage. In almost all cases, universities must license their rights in the early stage inventions and discoveries to an industry partner (whether an established company or a newly formed startup) to continue developing this invention or discovery until it is ready to be distributed to the public as a products or service. To manage this process, universities have

established technology transfer offices to assess new invention reports, manage intellectual property protection, marshal resources to further de-risk new technologies, and attract and license industry partners.

In 2017 alone, America's universities were granted more than 6800 patents, created over 1000 startup companies, produced many new medical breakthroughs, and generated millions of dollars of economic benefit for the country.

While a license of a university invention or discovery to an industry partner is considered a tech transfer success, it is just one step along the path of translating research into a product or service. New technology requires a company to invest in further development, refinement, and often regulatory clearance – typically very significant investments. In most cases, an industry partner will not take this significant investment without the assurances that the eventual product will benefit from patent exclusivity. Our universities have a front seat to all of these steps, so we observe clearly how patents promote innovation, and see on a daily basis that companies will not invest in making a product unless there is a reasonable, predictable chance that patent that will protect their investment. In fact, unless there is legal protection available for an invention, such as a patent, a tech transfer project typically terminates, which means that the university is not working with a business partner bring the invention to the public.

While a university licensee may receive exclusive rights under the university's patent protection, that period of exclusivity is limited. In regulatory intensive fields, such as life sciences, that window of exclusivity can sometimes be just a few years (between the regulatory approval and the expiration of the patent term, which starts running when the patent application was applied for, subject to Hatch Waxman). Once the patent term expires, others are free to use, and improve upon, the patented technology. Without a robust patent system, industry partners would more frequently resort to trade secret protection for early stage medical diagnostic discoveries, thus keeping the technology out of the public domain and preventing others from using and improving upon the technology.

Questions for the Record for Mr. Rick Brandon
Senate Committee on the Judiciary
Subcommittee on Intellectual Property
Hearing on "The State of Patent Eligibility in America: Part II"
June 5, 2019

QUESTIONS FROM SENATOR BLUMENTHAL

1. Striking the appropriate balance between encouraging innovation and protecting consumers is a key goal of our patent system.
    a. **What impact will broadening the subject matter that can be patented have on industry?**
    b. **What impact will broadening the subject matter that can be patented have on consumers?**
    c. **Could these reforms increase consumer prices? If so, in what industries or on what products?**

The proposed language is actually intended to make predictable that scope, and to restore the proper, time-tested standards established under U.S. patent law before courts and the Patent Office attempted to implement the subjective, uncertain standards enunciated in the cases that would specifically be abrogated. The inventions precluded from patenting under this standard are ones that generally would have been considered patent eligible in the past. To the extent this may possibly be considered "broadening" the subject matter that meets Section 101 eligibility requirements, this will benefit our entire system, industry and consumers included. Where a discovery meets all the requirements of patentability (including under Sections 101, 102, and 103), patent protection will, for example, incentivize a company to invent and develop a product into something that it can sell to the public, to further its business. However, given the current unpredictability and narrowness of Section 101, we believe that industry is not working on products that it otherwise would.

With regard to consumers, we believe that fixing Section 101 to (a) make it more predictable and (b) set it at a proper level of filtering (again, with Sections 102 and 103 significantly limiting what is actually patented) will benefit consumers, as discussed in responses to other question posted by the Subcommittee, because where an invention is not commercially developed there is no product for the consumer to use or consume.

The issue of hindering research and development applies to industry and consumers alike, so it bears mentioning again, as discussed in responses to other questions posed by the Subcommittee, that there are various protections against patents being enforced against researchers and developers of technology, for example provided by Section 271(e) and the Hatch-Waxman system. (Though AAU would support an inquiry into a broad research exemption that we currently do not have under U.S. law.)

Universities with health systems share the concerns that have been expressed about patient access to breakthrough medical technologies. AAU agrees that our system should strike an appropriate balance between encouraging innovation and protecting consumers once a new product has been brought to market. As stated previously, indeed, we are fully aligned on this topic with groups advocating for broad patient access and affordability. However, the question

of broad access to a technology only becomes relevant once the technology has been brought to market. And since the patentability of medical diagnostics is unpredictable, there are technologies that are not being brought to market in the first place. Patients have no access to these technologies at all.

While AAU has not gathered or analyzed specific data, it would agree that in general where a product is patented, there could be a general tendency to affect pricing. This may possibly be more likely in the medical fields and/or single patent products, but by no means is this always the case. Many patented products directly compete against other patented products, even in the medical field.

We do not believe it is legitimate to criticize the patent system by looking at the price of existing patented products. Patents promote and incentivize investment in the creation, development, and bringing to market of new technology, as recognized in the U.S. Constitution. An inventor or developer's investment is made as a first step or steps – steps taken based on the inventor or developer in reliance upon the limited period of exclusivity provided by a patent. It is only after the inventor or developer's product is brought to market that she/he/it receives the promised benefit of the limited period of exclusivity. It is simply not legitimate to ignore the investment the patent prompted, and criticizing the reward that was promised for the investment. Robert Armitage powerfully made the point in his testimony to this Subcommittee:

> "Patents become the *sine qua non* of the ability to make the investments, to put new medicines into the clinic and get them to patients. So, it turns out that the price charged by a drug company for a drug that has no patents is zero because the drug doesn't get to market. On the other hand, if you're on the patient side of this equation, that drug is not available to the patient at any price; no matter how promising it might otherwise have been, the cost to the patient in rough terms is essentially infinite."

Questions for the Record for Rick Brandon
From Senator Mazie K. Hirono

1. Last year, Judge Alan Lourie and Judge Pauline Newman of the Federal Circuit issued a concurring opinion to the court's denial of *en banc* rehearing in *Berkheimer v. HP Inc.*, in which they stated that "the law needs clarification by higher authority, perhaps by Congress, to work its way out of what so many in the innovation field consider are § 101 problems."

Do you agree with Judges Lourie and Newman? Does § 101 require a Congressional fix or should we let the courts continue to work things out?

AAU believes that the situation demands a legislative fix. The complicated framework of the *Alice* and *Mayo* decisions have muddied the waters and threaten to derail many legitimate new technologies that could benefit our nation. Patent examiners and courts have often been put in an untenable spot in trying to figure what sort of inventions are patentable. And many U.S. patents have been invalidated on Section 101 grounds that are thinly-veiled prior art rejections based on limited analysis. The opportunities we have to develop inventions cannot wait on the uncertain treatment (or even opportunity for treatment) by the courts. The Supreme Court has refused to reconsider its Section 101 rulings 42 times (denying *certiorari*). Only Congress can correct the situation.

But even more important than AAU's view are the views of our nation's foremost leaders on patent issues, especially PTO Directors and current and Federal Circuit judges. Former Chief Judge Michel testified to this Subcommittee that he could not predict eligibility in any given case, saying, "If I can't do it, how can bankers, venture capitalists, business executives and all the other players in the system make reliable predictions and sensible decisions?" As for whether the solution lies with the courts or Congress, Judge Michel added that the Federal Circuit has "fallen down on the job" and "legislation is the only solution. The Supreme Court has turned down every cert petition; they've no intention of straightening out the problem." (27th Intellectual Property Law & Policy Conference, April 22, 2019.)

Former PTO Director Q. Todd Dickinson testified that neutral stakeholder organizations and Federal Circuit judges and "have repeatedly stated that they cannot figure out what the Supreme Court meant in these cases or that they have led to inequitable results, and that Congress needs to exercise its Constitutional duty to legislate in this area. As I indicated above, I join that in that call." Although current PTO Director Andrei Iancu has done a great job in revising Section 101 subject matter eligibility guidance and training examiners, in the April's *Cleveland Clinic Foundation* decision, the Federal Circuit explicitly stated that it was "not bound" by the Guidance of the PTO, creating conflict between the courts and the executive branch. To quote former PTO Director David Kappos, Section 101 an "irreconcilable mess." A legislative fix is needed.

2. The Federal Circuit rejected a "technological arts test" in its *en banc Bilski* opinion. It explained that "the terms 'technological arts' and 'technology' are both ambiguous and ever-changing." The draft legislation includes the requirement that an invention be in a "field of technology."

a. Do you consider this a clear, understood term? If so, what does it mean for an invention to be in a "field of technology"?

b. The European Union, China, and many other countries include some sort of "technology" requirement in their patent eligibility statutes. What can we learn from their experiences?

c. Is a claim that describes a method for hedging against the financial risk of price fluctuations—like the one at issue in the *Bilski* case—in a "field of technology"? What if the claim requires performing the method on a computer?

d. What changes to the draft, if any, do you recommend to make the "field of technology" requirement more clear?

AAU has not studied alternatives or refinements to the term "field of technology," but wonders whether the term may be somewhat ambiguous, especially in being unclear on its face as to whether it would include business methods such as the one at issue in *Bilski*. Without further clarification, we worry that this phrase may reintroduce the type of uncertainty that the proposal was intended to overcome. Unless there is an intent to remove specific areas of invention/discovery, it would seem that the language would work well by simply removing this term.

3. Sen. Tillis and Sen. Coons have made clear that genes as they exist in the human body would not be patent eligible under their proposal.

Are there other things that Congress should make clear are not patent eligible? There are already statutes that prevent patents on tax strategies and human organisms. Are there other categories that should be excluded?

AAU is not aware of other subject matter that should be patent ineligible. We would be happy to work with the Subcommittee by reviewing any proposals; although Congress has made tax avoidance schemes and patents on human beings ineligible by statute, and has excluded from patent infringement the practice of a medical method claim by medical personnel, such proscriptions should be used sparingly, in ways that do not create uncertainty across broad swaths of American innovation.

4. I have heard complaints that courts do not consistently enforce Section 112 with respect to claims for inventions in the high tech space.

a. Are these valid complaints?

b. Do the proposed changes to Section 112 adequately address those complaints and limit the scope of claims to what was actually invented?

c. Are you concerned that the proposed changes will make it too easy for competitors to design around patent claims that use functional language?

AAU would be happy to work with the Subommittee in the future to address this issue with more specificity. We did pose questions regarding with the Section 112 language in our written testimony, and think that probably some revision or clarification would be helpful. For example, we wonder how this would work with method claims. We are also concerned with any change in the law that would promote the recitation in patent specifications of long, rote lists of "structure,

material, or acts." Such a practice may put even further pressure on patent examiners, delay or impede patent filings, favor large filers over small companies and individuals, push applications to more resemble a manufacturing specification than was ever intended, or other unintended consequences. Ultimately, our initial view is that although we understand a fix to Section 101 may require buy-in of a variety of stakeholders and we do not want to delay the fix, we do not currently believe that current Section 112(f) requires an expansion, as the proposed language would seem to do. As Judge Michel testified, "all functional terms cannot be entirely avoided, particularly in method claims and health sciences. The discussion draft's alteration of 112(f) automatically pushes all such inventions into that provision."

5. There is an intense debate going on right now about what to do about the high cost of prescription drugs. One concern is that pharmaceutical companies are gaming the patent system by extending their patent terms through additional patents on minor changes to their drugs. My understanding is that the doctrine of obviousness-type double patenting is designed to prevent this very thing.

The Federal Circuit has explained that obviousness-type double patenting "is grounded in the text of the Patent Act" and specifically cited Section 101 for support.

Would the proposed changes to Section 101 and the additional provision abrogating cases establishing judicial exceptions to Section 101 do away with the doctrine of obviousness-type double patenting? If so, should the doctrine of obvious-type double patenting be codified?

We agree that the effects on obviousness-type double patenting must be considered, possibly resulting in the codification of the judicially-created doctrine. However, we do not follow the criticism that minor, unpatentable changes to products, such as pharmaceuticals, are being used to extend patent terms. For example, if a second patent claims priority to a first patent, then under current (20-year-from-filing term) law, the second patent will expire on the same day as the first patent (subject to patent term adjustment or extension, which are different issues entirely). If a second patent does not claim priority to a first patent, then (assuming current obviousness-type double patenting law applies) the claims in the second patent would have to be patentably distinct from the first. Changes to FDA rules could perhaps avoid any real problems associated with "product hopping" or "evergreening," however we have not seen a problem within the patent system itself.

6. In its *Oil States* decision, the Supreme Court explicitly avoided answering the question of whether a patent is property for purposes of the Due Process Clause or the Takings Clause.

What are the Due Process and Takings implications of changing Section 101 and applying it retroactively to already-issued patents?

AAU agrees that this is an important issue, but we have not yet formulated a position on it. We would be willing to work with the Subcommittee and consider future proposals.

Attachment A
Exact Sciences Corporation

Exact Sciences Corporation is a molecular diagnostics company focused on the early detection and prevention of some of the deadliest forms of cancer. Exact Sciences recognizes that, too often, cancer is detected too late. We are committed to using our expertise and determination to help detect cancer earlier, when outcomes are better and treatment is less costly. To achieve this, we are working to deliver life-changing innovations in earlier cancer detection to help people make more effective and timely decisions. In collaboration with the Mayo Clinic, we are developing tests for the fifteen deadliest cancers and aim to bring people simple and accurate tests that solve significant clinical problems.

The first result of our efforts is the development and launch of Cologuard® (multi-target stool DNA, or mt-sDNA), a non-invasive stool-based DNA screening test that utilizes multiple biomarkers to detect DNA and hemoglobin biomarkers strongly associated with colorectal cancer and pre-cancer. Methylation, mutation, and hemoglobin results are combined in the laboratory analysis through a proprietary algorithm to provide a single positive or negative reportable result. In August 2014 the U.S. Food and Drug Administration granted premarket approval to Cologuard for use as a colorectal cancer screening test in adults 50 years of age and older who are at average-risk for colorectal cancer. Our submission to the FDA for Cologuard was supported by a 10,000-patient clinical trial.

The 20-year path to creating and commercializing a stool-based DNA test for colorectal cancer screening required a substantial investment. While some biomarkers are naturally occurring, their identification, extraction, and use to detect cancer and pre-cancer is a risky venture that requires the highest degree of innovation. Exact Sciences developed an earlier version of a stool-based DNA test from 1995 through 2008. Those efforts failed, and as of December 31, 2008 the company had an accumulated deficit of more than $172 million.

In 2009, Exact Sciences formed a collaboration with Mayo Clinic and began working on what is now Cologuard. From 2009 through Cologuard's FDA approval in 2014, we invested $128 million in Cologuard's development. The cost of the pivotal clinical trial alone was more than $35 million. Cologuard has helped more than 2 million people screen for colorectal cancer, nearly half of whom had never been screened before.

The strong foundation of Cologuard and our 10-year collaboration with Mayo Clinic now position Exact Sciences to lead in earlier cancer detection. Since 2009, the company has grown from a team of three to more than 2,400 employees across the United States. We are now working on the 15 deadliest cancer and aim to bring people simple and accurate tests that solve significant clinical problems.