No. 13-180

In the Supreme Court of the United States

W. SCOTT HARKONEN, PETITIONER

v.

UNITED STATES OF AMERICA

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

BRIEF FOR THE UNITED STATES IN OPPOSITION

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QUESTIONS PRESENTED

1. Whether petitioner, in issuing a press release intended to promote potential commercial uses of a drug, made a fraudulent statement within the scope of the wire-fraud statute, 18 U.S.C. 1343, about the results of a clinical trial.

2. Whether the wire-fraud statute violates the First Amendment or is unconstitutionally vague as applied to petitioner's conduct.

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OPINIONS BELOW

The judgment of the court of appeals (Pet. App. 1a-8a) is not published in the Federal Reporter but is reprinted in 510 Fed. Appx. 633. The district court's orders denying petitioner's motions in limine and to dismiss the indictment (Pet. App. 55a-81a) and denying post-trial relief (Pet. App. 9a-54a) are available at 2009 WL 1578712 and 2010 WL 2985257.

JURISDICTION

The judgment of the court of appeals was entered on March 4, 2013. A petition for rehearing en banc was denied on May 7, 2013 (Pet. App. 82a). The petition for a writ of certiorari was filed on August 5, 2013. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

Following a jury trial in the United States District Court for the Northern District of California, petitioner was convicted on one count of wire fraud, in violation of 18 U.S.C. 1343. Pet. App. 9a. He was sentenced to three years of probation and a $20,000 fine. *Id.* at 2a. The court of appeals affirmed. *Id.* at 1a-8a.

1. Petitioner was the Chief Executive Officer and Chairman of the Board of Directors of the biopharmaceutical company InterMune, Inc. Pet. App. 10a; Gov't C.A. Br. 5. In August 2002, petitioner issued a fraudulent press release touting the results of a clinical trial of Actimmune, the drug that was InterMune's principal source of revenue. Pet. App. 2a, 10a-11a; Gov't C.A. Br. 23-24. The press release included an analysis of the clinical data purportedly demonstrating that the drug significantly reduced mortality rates in certain patients, without disclosing that the analysis had been generated in a manner that the unconstested evidence at trial showed to be unreliable. Pet. App. 19a-30a. Even petitioner himself "was 'very apologetic' about the Press Release's misleading nature." *Id.* at 3a.

a. Actimmune had previously received approval from the Food and Drug Administration (FDA) as a treatment for two rare pediatric diseases. Pet. App. 10a. The press release attempted to promote Actimmune in a different, and potentially much more lucrative, market as a treatment for idiopathic pulmonary fibrosis (IPF). *Ibid.*; see *id.* at 86a; Gov't C.A. Br. 6. IPF is a fatal disease with no known cure and is "characterized by progressive scarring, or fibrosis, of the lungs which leads to the lung[s'] deterioration and destruction." Pet. App. 10a. Although the FDA had

not approved Actimmune as a treatment for IPF, the absence of such approval would not preclude a doctor from prescribing Actimmune for that purpose. Gov't C.A. Br. 7 n.4.

In 1999, a small Austrian study of 18 people—the methodology of which was later called into question—suggested that Actimmune might have beneficial effects for IPF patients. Gov't C.A. Br. 6 & n.2. In 2000, InterMune launched its own clinical trial (the GIPF-001 Phase III trial) to determine Actimmune's efficacy and safety as an IPF treatment. *Id.* at 6-7. Petitioner recognized during a company-wide national sales meeting in July 2001 that "the market opportunity here is 2 and a half billion," and he saw "no reason we shouldn't capture 40% of this market and turn Actimmune into a billion dollar revenue producer." *Id.* at 6. Every patient taking Actimmune for IPF would pay approximately $50,000 a year for the drug. *Ibid.*

The GIPF-001 trial "was a randomized, double-blind, placebo-controlled trial," which "represent[s] the gold standard for determining the relationship between a drug and a health outcome." Pet. App. 15a (internal quotation marks omitted). In such a trial, some patients receive the drug being tested, while others receive a placebo, and neither the patients nor the researchers know who gets which. *Id.* at 15a-16a.

Before beginning such a trial, "researchers set forth a detailed study protocol, which includes, among other things, the objectives of the study (i.e., what causal relationships the study is attempting to measure), the inclusion and exclusion criteria for determining who will be allowed to participate in the trial, the procedures for administering the treatment and re-

cording results, and specifications for how the data from the study will be analyzed." Pet. App. 16a. Although the protocol sometimes changes during the course of the trial, "a final protocol must be in place before the study's data is 'unblinded' (i.e., made available) to the study's researchers." *Ibid.* Predetermining both the "objectives (or 'endpoints' as they are typically called)" and the "criteria for how the data will be analyzed (known as a 'statistical analysis plan')" is "crucial for maintaining the integrity of the study." *Id.* at 16a. In particular, it precludes researchers "from manipulating the data after it is 'unblinded' in order to identify a favorable result." *Id.* at 16a-17a.

The pre-unblinding protocol developed for the GIPF-001 trial had one "primary endpoint" (*i.e.*, desired result): patients living without any worsening of their lung capacity ("progression-free survival"). Pet. App. 17a. The protocol also identified ten "secondary" endpoints, listed in order of clinical relevance, along with eight tertiary or "exploratory" endpoints. *Ibid.*; Gov't C.A. Br. 8. The seventh-ranked secondary endpoint was "survival" or "mortality"—*i.e.*, patients not dying while taking the medicine. Pet. App. 17a-18a; Gov't C.A. Br. 9-10. Survival was ranked seventh partly based on concern that the trial would include too few deaths to enable a reliable statistical analysis. Gov't C.A. Br. 10.

b. When Dr. Michael Crager, InterMune's chief biostatistician, received the results from the GIPF-001 trial, "it was immediately apparent that the study had missed its primary endpoint as well as all ten of the secondary endpoints." Pet. App. 18a, 23a. As explained by Dr. Thomas Fleming, a noted biostatisti-

cian and chair of the clinical trial's Data Monitoring Committee (an outside group of experts selected by InterMune), "the results were entirely consistent with [Actimmune having] no effect." Gov't C.A. Br. 12 (emphasis omitted); see Pet. App. 18a; C.A. Supp. E.R. 418.

According to Dr. Crager's and Dr. Fleming's testimony, the significance of a trial's results is primarily expressed through the p-value, which is a number between zero and one. Pet. App. 18a-19a. The lower the p-value, the greater the probability that the result reflected by the data is meaningful and not due to chance. *Id.* at 19a. For example, a p-value of 0.05 indicates that, if the drug in the trial had no effect on the outcome, the data obtained in the trial would occur by chance less than five percent of the time. *Ibid.* As a general matter, if the p-value for the primary endpoint is less than or equal to 0.05, then the results on the primary endpoint are considered statistically significant; if greater than 0.05 the results are generally considered unreliable and not statistically significant. *Ibid.* InterMune adopted the 0.05 p-value as the standard for statistical significance in this trial. C.A. Supp. E.R. 437-439.

Drs. Crager and Fleming also explained, however, that to properly interpret whether a p-value for a particular endpoint renders that endpoint statistically significant, "it is necessary to know the context in which that p-value was generated." Pet. App. 19a. First, one needs to know the number of endpoints, because, under a principle known as the "multiplicity effect," the results for any one endpoint become less statistically reliable the greater the number of secondary and tertiary endpoints. *Id.* at 20a. Dr. Flem-

ing analogized this to wanting to know, in evaluating the significance of a marksman hitting a target, how many shots the marksman took overall. *Id.* at 20a-21a. Second, one needs to know whether the primary endpoint has failed, because the failure of the primary endpoint suggests that the experiment's basic hypothesis about the mechanism through which a drug might achieve positive results (*e.g.*, that Actimmune prolongs IPF patients' lives by inhibiting lung deterioration) is false, thereby casting doubt on whether any positive secondary result (*e.g.*, that patients taking Actimmune have a higher survival rate) actually reflects a causal relationship. *Id.* at 21a-22a. Third, one would want to know whether the analysis was part of the pre-specified research protocol, or instead a p-value calculated after unblinding, because post hoc analyses are, Dr. Fleming testified, "typically very unreliable." *Id.* at 22a-23a. Accordingly, even a p-value below 0.05 for secondary, tertiary, and post hoc endpoints may not be statistically significant. *Id.* at 19a-23a.

Here, the p-value for the GIPF-001 primary endpoint—progression-free survival—turned out to be 0.52, which was "far too high to demonstrate any statistically significant correlation" between Actimmune and progression-free survival. Pet. App. 23a-24a. None of the secondary endpoints produced a p-value below 0.05, either. *Id.* at 26a. According to InterMune's own internal predictions about the impact of study results on revenue, this was its worst case scenario. C.A. Supp. E.R. 2488-2496. Indeed, when the results were unblinded, petitioner called InterMune's general counsel to tell him that the data "really wasn't looking very good." *Id.* at 2862.

When he first reviewed the results, Dr. Crager did note that, for the seventh secondary endpoint (survival), the analysis suggested a 40% decrease in mortality, with a p-value of 0.084. Pet. App. 24a. Dr. Crager accordingly suggested to petitioner that the data might serve as the basis for a trial with survival as the primary endpoint. *Ibid.*; see *id.* at 23a. However, Dr. Crager saw "no apparent way from the data that the drug would be working," given the absence of any indication that it actually improved lung function, C.A. Supp. E.R. 1974, and he explained to petitioner that "we don't have any evidence of how" the drug would be increasing survival rates, *id.* at 1989.

c. Dr. Crager subsequently requested a post hoc analysis of the survival time for subgroups of patients with relatively high lung function. Pet. App. 24a. As Dr. Fleming explained to the jury (and as Dr. Crager himself corroborated), the post hoc analysis of endpoints not prespecified in the trial protocol "is of use for exploring future hypotheses to test as a primary or secondary endpoint, but has limited if any conclusive power." *Id.* at 22a. Dr. Fleming testified that such analyses are "notoriously unreliable" and that "almost any trial" could obtain a p-value below 0.05 through a "multiplicity of testing by multiple analyses over time, by multiple study endpoints." *Ibid.*

The subgroup results indicated that only three of the 90 patients treated with Actimmune in the subgroup Dr. Crager selected had died during the study, while 12 of 92 patients with worse lung functioning had died, yielding a p-value of 0.024. Pet. App. 24a-25a. Upon learning this, petitioner ordered Dr. Crager to conduct additional analyses of mortality by breaking the population into three subgroups—mild,

moderate, and severe IPF patients—the precise definitions of which were selected by InterMune. *Ibid.*; see C.A. Supp. E.R. 230, 612-613, 2508-2509 (explaining that those subgroups do not have precise generally-accepted definitions). After Dr. Crager delivered the results of that second post hoc analysis, petitioner instructed Dr. Crager to run a third post hoc analysis that would combine the mild and moderate IPF patients into one group. Pet. App. 25a. Petitioner indicated that "they were going to have Michael Crager cut that data and slice it until they got the kind of results they were looking for." C.A. Supp E.R. 2509.

On the third run through the data, only six of the 126 (4.8%) participants treated with Actimmune in the "mild to moderate" group died during the clinical trial, compared to 21 of the 128 (16.4%) patients in the corresponding placebo group, a result that suggested a 70% reduction in mortality and yielded a p-value of 0.004. Pet. App. 25a-26a. Significantly, however, this analysis defined the subgroups in such a way that patients with severe IPF had a *higher* deathrate if they had used Actimmune than if they had used the placebo—not what one would expect to see if Actimmune truly helped IPF patients live longer. Gov't C.A. Br. 26; see C.A. Supp. E.R. 464-465 (Dr. Fleming's testimony).

Petitioner directed that some, but not all, of the post hoc subgroup analyses be faxed to the FDA. Gov't C.A. Br. 17. Petitioner told Dr. Crager not to send all of the post hoc analyses "because we didn't want to make it look like we were doing repeated analyses [of the same endpoint] looking for a better result." *Ibid.* (brackets in original).

d. Petitioner was informed by multiple other people on multiple other occasions that the trial had failed and that the post hoc analysis was unreliable and inconclusive. Pet. App. 34a-36a. First, at a meeting between InterMune management and the Data Monitoring Committee, Dr. Fleming told petitioner that the trial results indicated that Actimmune had no effect on slowing the progression of IPF and that none of the secondary endpoints achieved a statistically significant p-value. C.A. Supp. E.R. 447-449. As a result, "there was quite a strongly reinforced insight that Actimmune had not provided evidence or the trial had not provided evidence that Actimmune provides a clinically-meaningful effect." *Id.* at 448-449. After Dr. Fleming expressed his views, which were shared by the other committee members, *id.* at 450, petitioner instructed that Dr. Fleming be disinvited from participating in a subsequent call with the FDA, as well as a steering committee meeting, Gov't C.A. Br. 18.

Second, Dr. Steven Porter, InterMune's Senior Vice President of Clinical Affairs and Chief Medical Officer, discussed with petitioner the "disappointing" trial results and that "[i]t was impossible to know whether these findings [the secondary endpoint of survival and the subgroup analysis] were real or not." C.A. Supp. E.R. 1131, 1133-1336; see Pet. App 35a; see also C.A. Supp. E.R. 1131 (Dr. Porter's testimony that he told petitioner "it was impossible to tell whether" the "observations on survival" were "chance or real"). Third, Dr. Marc Walton from the FDA informed petitioner on a conference call that because "the physiologic measurements did not show any apparent treatment effect, the decrease in mortality in his opinion could be considered 'almost an anomalous finding in

the face of no effect on pulmonary function and so warrants extra caution.'" Pet. App. 35a. Dr. Walton additionally informed petitioner that "there was no way to give [the survival data] a meaningful p-value in the face of the failed primary endpoint." *Id.* at 35a (brackets in original).

e. At the same time that he was receiving this information, petitioner was preparing a press release interpreting the GIPF-001 trial results as "appear-[ing] to confirm" the survival benefit inconclusively suggested by the original Austrian study. Pet. App. 86a-87a. Petitioner "was the controlling force behind the content of the press release," *id.* at 26a, which was, according to the company's general counsel, the most important in the company's history, Gov't C.A. Br. 20.

In a departure from normal procedure, petitioner severely restricted access to the press release before it was issued. Pet. App. 36a-38a. Petitioner allowed no one with a clinical or statistical background or who had reviewed the clinical trial data to review a complete draft of the press release. *Id.* at 37a. At the same time, petitioner misled the firm's general counsel into believing that InterMune's clinical and regulatory staff had reviewed the release. Gov't C.A. Br. 23.

The headline of the press release stated: "InterMune Announces Phase III Data Demonstrating Survival Benefit of Actimmune in IPF." Pet. App. 84a. The subheading read: "Reduces Mortality by 70% in Patients with Mild to Moderate Disease." *Ibid.* The press release included a quote by petitioner stating that "Actimmune is the only available treatment demonstrated to have clinical benefit in IPF"; that the trial results "will support use of Actimmune" as an

IPF treatment; and that such use would "lead to peak sales in the range of $400-$500 million per year, enabling us to achieve profitability in 2004 as planned." *Id.* at 85a. In addition to stating that the data "appear[ed] to confirm" the original Austrian study, *id.* at 86a, the press release touted the "significant survival benefit" demonstrated by Actimmune in patients with mild to moderate IPF, reporting a p-value of 0.004 and characterizing the result as "statistically significant," *id.* at 84a. The press release did not make "any adjustment for context, including for secondary endpoints and post-hoc analyses." *Id.* at 28a-29a.

While the press release acknowledged that the study's primary endpoint was not statistically significant, it did not inform readers that the study had also missed all of its secondary endpoints. Pet. App. 85a; see *id.* at 25a. Rather, the acknowledgement regarding the missed primary endpoint was immediately followed by a statement that "[i]mportantly, Actimmune also demonstrated a strong positive trend in increased survival in the overall patient population, and a statistically significant survival benefit in patients with mild to moderate IPF." *Id.* at 86a. The press release omitted "any mention that the only results with a p-value less than 0.05 * * * were observed only after InterMune engaged in retrospective analysis," and it did "not explain that the study protocol set out ten secondary endpoints—of which survival time was ranked as only the seventh most clinically relevant—and that all ten failed to produce statistically meaningful results." *Id.* at 29a.

When Dr. Fleming first read the press release after it was issued, he was "stunned," finding it to be "a serious misrepresentation of the truth as [he] under-

stood it." Gov't C.A. Br. 26 (brackets omitted). He wrote a letter to InterMune harshly criticizing the press release. *Ibid.* When petitioner met with the chair of the steering committee responsible for designing the trial, petitioner was "very apologetic" about the press release and provided assurances that he would issue a second press release and that the "record w[ould] be set straight." C.A. Supp. E.R. 644, 646; Pet. App. 3a.[1] Although InterMune did eventually issue a second press release, it never retracted the first one, which InterMune's sales force continued to use to promote Actimmune as a treatment for IPF. Gov't C.A. Br. 27.

2. A grand jury indicted petitioner on one count of misbranding of Actimmune, in violation of 21 U.S.C. 331(k), 333(a)(2) and 352(a), and one count of wire fraud, in violation of 18 U.S.C. 1343. Gov't C.A. Br. 4. The wire-fraud statute prohibits anyone who has "devised or intend[s] to devise any scheme or artifice to defraud" from making a wire transmission in interstate commerce "for the purpose of executing such scheme or artifice." 18 U.S.C. 1343.

Petitioner moved to dismiss the indictment on First Amendment grounds. Pet. App. 55a. Recognizing that the "the First Amendment does not shield fraud," the district court denied the motion. *Id.* at 63a (quoting *Illinois* v. *Telemarketing Assocs., Inc.*, 538

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[1] The press release had included a quote from the steering-committee chair, Dr. Ganesh Raghu, stating that "[t]he mortality benefit is very compelling." Pet. App. 85a; see Gov't C.A. Br. 10. Dr. Raghu explained that he did not have the actual data from the clinical trial before the press release and that he made that statement based on petitioner's positive description of the data. Gov't C.A. Br. 25 n.14.

U.S. 600, 612 (2003)); see Pet. App. 55a-81a. The jury found petitioner guilty on the wire fraud charge and acquitted him on the misbranding charge. Gov't C.A. Br. 5.

The district court denied petitioner's motion for post-trial relief, recognizing that "the government met its burden of proof, and did so convincingly." Pet. App. 39a; see *id.* at 9a-54a. The district court found "sufficient evidence for the jury to conclude beyond a reasonable doubt that multiple statements contained in the press release were false or fraudulent." *Id.* at 27a-28a. First, the jury could validly have found that the press release's headline (which claimed that the Phase III data "demonstrat[ed] a survival benefit") was "objectively untrue," in light of testimony that the secondary endpoint of survival failed to achieve statistical significance. *Id.* at 28a. Second, "the jury could have found that [petitioner's] choice of words in the press release implied causation between Actimmune and the survival of IPF patients, when the data from the study objectively did not establish any such certain and/or verifiable relationship," in light of the "credible testimony that in clinical trials with multiple endpoints, where the primary endpoint is missed, and where researchers conduct post-hoc subgroup analyses, p-values are unreliable." *Id.* at 28a. The court observed that this "falsity" was "[m]agnif[ied]" by the "complete omission" of any acknowledgment that the reported p-values were the result of post hoc analysis and that "at the time of the press release there was no publically available data for the GIPF-001 such that interested individuals could verify the results." *Id.* at 29a. Finally, the jury could have concluded that the press release "as a whole" was false or fraudulent, in

that it "describe[d] the study as a success" when "the overwhelming, undisputed evidence at trial" showed that the "study was a failure," in that it "missed its primary endpoint as well as all ten secondary endpoints." *Id.* at 30a. The court acknowledged that a pharmaceutical company is permitted to put a "positive spin" on the results of a clinical trial, so long as it is done with "candor and disclosure," but stressed that "the jury could have found that the press release [here] was so optimistic, in the face of the trial's objective failure, that it constituted fraud." *Id.* at 30a.

The district court also found sufficient evidence of knowledge of falsity and intent to defraud. Pet. App. 34a-38a. The court recounted testimony showing that petitioner was informed that the trial had missed all its primary and secondary endpoints and that the post hoc subgroup analyses were unreliable. *Id.* at 34a-36a. It also noted that "the efforts engaged in by [petitioner] to prevent certain individuals, both outside and inside InterMune, from reviewing the press release serves as powerful circumstantial evidence of his intent to defraud, as well as his knowledge of falsity." *Id.* at 36a. The court additionally emphasized petitioner's strong financial motivation to portray the clinical trial as a success. *Id.* at 36a-38a.

Based on the evidence of petitioner's fraud, and again recognizing that "the First Amendment does not protect fraud," the district court also rejected petitioner's renewed argument that his statements were protected by the First Amendment. Pet. App. 40a (internal quotation marks and citations omitted). The district court also rejected petitioner's argument that his conviction violated due process because he lacked fair notice that his conduct was criminal. *Id.* at 41a-

44a. The court explained that "[t]o contend that [petitioner] was not on notice that [he might face wire-fraud liability] if he lied in a press release about the success of [a] clinical trial for a drug that might have sales as high as $500 million per year is simply ludicrous." *Id.* at 42a. Petitioner was sentenced to three years' probation, with six months of home confinement, and a $20,000 fine. Gov't C.A. Br. 5.

3. The court of appeals affirmed in an unpublished memorandum opinion. Pet. App. 1a-8a.

The court rejected petitioner's First Amendment challenge to his conviction. Pet. App. 2a-6a. The court reviewed that challenge in two steps: (1) a deferential review of the sufficiency of the evidence, and (2) a determination "whether the facts, as found by the jury, establish the core constitutional facts." *Id.* at 2a. The court explained that because "the First Amendment does not protect fraudulent speech," *ibid.* (citing *United States* v. *Alvarez*, 132 S. Ct. 2537, 2544 (2012) (plurality opinion)), "the core constitutional issue" was "whether the facts the jury found establish that the Press Release was fraudulent," *id.* at 2a-3a.

On the first step, the court of appeals found sufficient evidence to support the conviction. Pet. App. 3a-4a. It observed, *inter alia*, that "[a]t trial, nearly everybody actually involved in the GIPF-001 clinical trial testified that the Press Release misrepresented GIPF-001's results," *id.* at 3a; that petitioner had stated his intent to "cut the data and slice it until he got the kind of results he was looking for," *id.* at 4a (internal quotation marks omitted); and that even petitioner himself had been "'very apologetic' about the Press Release's misleading nature," *id.* at 3a. On the second step, the court determined that, "upon

independent review of the record," petitioner's conviction satisfied the First Amendment. *Id.* at 5a. The court of appeals explained that, "[c]ritically," petitioner "presented the evidence that most firmly supported his case" (namely, expert declarations regarding the significance of p-values and post-hoc subgroup analyses, see Gov't C.A. Br. 51) "for the first time at sentencing." Pet. App. 5a n.2. The court of appeals declined to "reverse the jury's verdict based on evidence it never considered." *Ibid.*

The court of appeals next rejected petitioner's argument that the press release was part of a "genuine debate[]" about the efficacy of a drug and should thus fall outside the scope of the wire-fraud statute. Pet. App. 5a-6a. The court of appeals acknowledged that "genuine debates of any sort are, by definition, not fraudulent," but reasoned that petitioner's "request that we reverse his conviction because he was engaging in a genuine scientific debate is hardly different than arguing that he is innocent." *Id.* at 6a. The court further observed that the government need not prove, as a prerequisite to fraud liability, that a statement is "universally considered objectively false," but instead need only prove that it involves a "'dishonest method or scheme,'" or "any 'trick, deceit, chicane or overreaching.'" *Id.* at 5a-6a (quoting *Carpenter* v. *United States*, 484 U.S. 19, 27 (1987)) (brackets omitted). The court of appeals concluded, contrary to petitioner's contention, that *American School of Magnetic Healing* v. *McAnnulty*, 187 U.S. 94 (1902), "does not categorically prohibit fraud prosecutions for statements about the efficacy of a particular drug," noting that this Court has in fact deemed it "'obvious'" that "'false and fraudulent representations may be made

with respect to the curative effect of substances.'" Pet. App. 5a (quoting *Seven Cases* v. *United States*, 239 U.S. 510, 517 (1916)).

The court of appeals additionally rejected petitioner's due process argument, noting that it "is essentially a re-dressing of his First Amendment and *McAnnulty* arguments, so it too must fail." Pet. App. 6a. The court concluded that "[a]n ordinary person would have understood that if he made misleading statements in a press release with the specific intent to defraud he would be subject to the wire fraud statute." *Ibid.* (internal citation omitted).

ARGUMENT

Relying on a characterization of the record that the court of appeals expressly rejected as tantamount to a claim of factual innocence—namely, that he was convicted merely for drawing a "conclusion" about which "scientists may reasonably disagree," Pet. i—petitioner contends (Pet. 15-35) that his wire-fraud conviction exceeded the scope of 18 U.S.C. 1343, violated the First Amendment, and was inconsistent with due process. Those contentions lack merit. The court of appeals correctly affirmed petitioner's conviction; its result and reasoning do not conflict with any decision of this Court or any other court of appeals; and no further review of its unpublished memorandum disposition is warranted.

1. a. As both courts below correctly concluded, the record in this case was sufficient to convict petitioner of wire fraud, in violation of 18 U.S.C. 1343. The evidence showed that petitioner, despite being repeatedly told that the GIPF-001 trial was a failure, ordered that the unblinded clinical trial data be re-analyzed multiple times in a search for any positive result to

report. Pet. App. 3a-4a; 13a-38a. When he finally found what he was looking for, he crafted a press release—which he did not allow his scientists to review—portraying the double-blind trial as a success. *Id.* at 26a, 36a-38a, 84a-90a. The press release touted "a statistically significant survival benefit" in certain patients that "appear[ed] to confirm" the earlier suggestion of the Austrian study. *Id.* at 86a. The press release did not provide any indication that the reported positive results were the product of the sort of unblinded post hoc analysis that, according to the evidence, is generally considered to be unreliable. *Id.* at 84a-90a; see *id.* at 19a-23a.

Even assuming individual statements in the press release could be deemed literally true in isolation, the jury was entitled to conclude that, in context, and in light of what was omitted, petitioner's statements were misleading. See *Donaldson* v. *Read Magazine, Inc.*, 333 U.S. 178, 188-189 (1948) ("Advertisements as a whole may be completely misleading although every sentence separately considered is literally true. * * * Questions of fraud may be determined in the light of the effect advertisements would most probably produce on ordinary minds."). As the court of appeals observed, "[a]t trial, nearly everybody actually involved in the GIPF-001 clinical trial testified that the Press Release misrepresented GIPF-001's results," and even petitioner himself "was 'very apologetic' about the Press Release's misleading nature." Pet. App. 3a.

b. Contrary to petitioner's assertion (Pet. 14), he was not convicted for "express[ing] a scientific conclusion about which reasonable minds can differ." The court of appeals in fact expressly acknowledged that

"genuine debates of any sort are, by definition, not fraudulent." Pet. App. 6a. Petitioner was convicted not for engaging in such debate, but instead for deliberately crafting a press release to mislead readers into believing that the reported result was a statistically significant conclusion of a double-blind trial, rather than a post hoc analysis generated only after intentional repackaging of the data. See *id.* at 20a-23a. The press release did not simply put a "positive spin" on results open to multiple interpretations, but lacked the basic "candor and disclosure" necessary to understand the unreliable methodology underlying the conclusions it presented. *Id.* at 30a.

To the extent that petitioner and his amici now claim that members of the scientific community would, in fact, have considered the press release an entirely non-misleading way of presenting the results of the study, they rely on facts outside the evidence heard by the jury. At trial, petitioner chose not to present a single witness qualified to discuss medical or statistical issues who disputed the testimony of the government witnesses on the unreliability of the post hoc subgroup analyses and the misleading nature of the press release. Gov't C.A. Br. 40-41, 58-59. Although petitioner later, at sentencing, submitted declarations that challenged some of the statements by the government's witnesses, those declarations were neither part of the defense's case nor subject to cross-examination. *Id.* at 51.[2] The court of appeals properly disregarded that evidence on the ground that it would be improper to "reverse the jury's verdict based on evidence it never considered." Pet. App. 5a n.2. It

[2] The same is true of a declaration petitioner submitted before trial in support of a motion to dismiss. See Pet. App. 70a.

would be similarly improper to overturn the jury's verdict based on representations about scientific standards that appear in the appellate briefs of petitioner and his amici, which likewise were not presented or tested at trial. In any event, the post-trial declarations at most took the view that a survival benefit was a defensible inference from inconclusive data. C.A. Supp. E.R. 1311-1312, 3852-3853, 3900-3901, 5240-5241, 5255-5256, 5259, 5446. That is not the same as saying—as the press release did—that the benefit had been proven by the data. Pet. App. 86a.

Petitioner also errs in characterizing this case (*e.g.*, Pet. 15) as a governmental effort to enforce compliance with the FDA's own scientific views. The two primary witnesses that presented evidence on proper practices in biostatistics were Drs. Crager and Fleming, both of whom worked directly with petitioner on the clinical trial at issue in this case. Pet. App. 18a-23a. Although Dr. Fleming happens also to be a special FDA consultant, he was a member of the clinical trial's Data Monitoring Committee and was not representing the FDA in his testimony in this case. In any event, if petitioner believed that the testimony of Drs. Crager and Fleming about scientific protocols (which was consistent with the testimony of other witnesses) simply presented contestable opinion on scientific principles, he should have introduced evidence to that effect at trial.

c. Petitioner's contention (Pet. 25-26) that the result in this case conflicts with either the government's brief, or this Court's decision, in *Matrixx Initiatives, Inc.* v. *Siracusano*, 131 S. Ct. 1309 (2011), is misconceived. In *Matrixx*, the government argued, and this Court held, that adverse event reports associated with

the use of a company's drug can be considered material information that the company is required to disclose, even if the adverse event reports do not provide statistically significant evidence that the drug causes harm. *Id.* at 1313-1314. Nothing in the Court's opinion, or the government submission, suggested that all statistically insignificant associations or effects noted in analysis of a study are automatically reasonable inferences or debatable matters of opinion. Rather, the Court disavowed any "attempt to define * * * what constitutes reliable evidence of causation," and instead noted that a variety of factors may be considered. *Id.* at 1319-1320. Petitioner makes no attempt to show that those factors favored him here. At all events, neither the Court's decision nor the government's brief remotely embraced the idea that drug manufacturers may misleadingly present the results of a clinical trial as conclusively positive when the evidence establishes they are not. That is the unlawful conduct for which petitioner was convicted in this case.

d. Petitioner is wrong to suggest (Pet. 15-16) that the court of appeals' decision conflicts with *American School of Magnetic Healing* v. *McAnnulty*, 187 U.S. 94 (1902). *McAnnulty* held that a civil mail-fraud statute permitting the postmaster to refuse to deliver fraudulent materials did not apply to materials about the ability of the mind to heal the human body, reasoning that the statute "evidently do[es] not assume to deal with mere matters of opinion upon subjects which are not capable of proof as to their falsity." *Id.* at 104; see *id.* at 100 n.1, 103. As just discussed, petitioner in this case was not convicted for stating an opinion "not capable of proof as to [its] falsity." In-

stead, he was convicted for presenting the results of a clinical trial in a manner deliberately designed to conceal the unreliable way in which those results were procured.

In any event, as the court of appeals correctly recognized (Pet. App. 5a), nothing in *McAnnulty* categorically immunizes statements relating to clinical drug trials from criminal liability for fraud. To the contrary, in a later case involving the misbranding of a drug as "'effective for pneumonia,'" this Court found it "obvious" that "false and fraudulent representations may be made with respect to the curative effect of substances." *Seven Cases* v. *United States*, 239 U.S. 510, 514, 517 (1916). The Court rejected the proposition that the seller of a drug has an unfettered "right to give his views regarding the effect of his drugs," explaining that "persons who make or deal in substances or compositions, alleged to be curative, are in a position to have superior knowledge and may be held to good faith in their statements." *Id.* at 517-518.

In subsequent cases, this Court has repeatedly reaffirmed that "a difference of opinion as to whether a product had any value at all d[oes] not bar a fraud order based on claims of far greater curative powers than the product could actually have." *Reilly* v. *Pinkus*, 338 U.S. 269, 273 (1949) (discussing *Leach* v. *Carlile*, 258 U.S. 138, 139 (1922)). In *Reilly* v. *Pinkus*, *supra*, for example, the Court rejected a broad reading of *McAnnulty* as "bar[ring] a finding of fraud whenever there is the least conflict of opinion as to curative effects of a remedy." 338 U.S. at 273-274. The Court instead concluded that an advertisement about a product's weight-reducing properties could be found fraudulent "even if we assume that medical

opinion is yet in a state of flux on this question." *Id.* at 274; see *id.* at 275 (declining to affirm postmaster's fraud finding due to procedural error).

e. This decision below also does not conflict with any of the decisions in other circuits cited by petitioner and his amici. Petitioner cites (Pet. 16-17) three Sixth and Eighth Circuit cases, the most recent of which is 85 years old, stating that fraud cannot be predicated on a difference of opinion or on opinions honestly held. See *Stunz* v. *United States*, 27 F.2d 575, 578-579 (8th Cir. 1928); *Bruce* v. *United States*, 202 F. 98, 105 (8th Cir. 1912); *Harrison* v. *United States*, 200 F. 662, 665 (6th Cir. 1912) (involving the sale of home appliances). As discussed, however, petitioner here was not convicted for stating his opinion on a debatable scientific matter, but for authoring a press release that intentionally presented an unjustifiably skewed subset of data in a manner calculated to mislead.[3] The court of appeals expressly recognized, in accord with the cases cited by petitioner, that "genuine debates of any sort are, by definition, not fraudulent." Pet. App. 6a.

Petitioner similarly errs in suggesting (Pet. 17-19), that the decision below conflicts with the Second Circuit's decision in *ONY, Inc.* v. *Cornerstone Therapeutics, Inc.*, 720 F.3d 490 (2013). That case addressed the circumstances in which "a statement in a scientific article reporting research results" can give rise to a claim of false advertising under the Lanham Act, 15

[3] The reliance of one of petitioner's amici on more recent Seventh Circuit decisions (none of which are wire-fraud prosecutions) for the proposition that "reasonable scientific opinions are not actionable if they are the subject of good faith debate," PhRMA Amicus Br. 15, is misplaced for similar reasons.

U.S.C. 1501 *et seq.* 720 F.3d at 492. The court held that "to the extent a speaker or author draws conclusions from non-fraudulent data, *based on accurate descriptions of the data and methodology underlying those conclusions*, on subjects about which there is legitimate ongoing scientific disagreement, those statements are not grounds for a claim of false advertising under the Lanham Act." *Id.* at 498 (emphasis added). Assuming the Second Circuit would apply that same standard to a wire-fraud prosecution, it would not benefit petitioner here. Unlike in *ONY*, where the "authors readily disclosed the potential shortcomings of their methodology," *ibid.*, the press release here did not contain "accurate descriptions of the data and methodology underlying [petitioner's] conclusions," *ibid.*, but instead withheld important information about the use of multiple rounds of unblinded post hoc analysis to obtain the desired results after the initial trial had failed. Cf. *id.* at 494-495 (noting that the authors in *ONY* published in a peer-reviewed journal before issuing a press release, and that the article had specifically addressed an objection based on "the retrospective nature of the study"). The Second Circuit's decision in *ONY* accordingly provides no basis for this Court to review the first question presented in this case.

2. Petitioner's argument (Pet. 21-27) that his conviction violates the First Amendment likewise does not warrant certiorari. This Court has repeatedly recognized that the First Amendment "does not shield fraud." *Illinois* v. *Telemarketing Assocs., Inc.*, 538 U.S. 600, 612 (2003); see, *e.g.*, *United States* v. *Alvarez*, 132 S. Ct. 2537, 2544 (2012) (plurality opinion); *United States* v. *Stevens*, 559 U.S. 460, 468 (2010).

Petitioner contends (Pet. 23), however, that even when sufficient evidence supports a jury's finding beyond a reasonable doubt that a defendant has made fraudulent statements, a defendant who invokes the First Amendment is entitled to independent and non-deferential judicial review of the record to ensure that the reviewing court would itself agree with the verdict. That contention lacks merit and does not warrant further review.

As a threshold matter, this case would be an unsuitable vehicle for reviewing that question. The court of appeals stated that it was, in fact, affirming petitioner's conviction "upon independent review of the record." Pet. App. 5a. Although petitioner now appears to believe that the court of appeals' review was too deferential to the jury, petitioner's brief in the court of appeals relied on circuit precedent as supplying the proper standard of review, see Pet. C.A. Br. 35, and the court of appeals drew its standard of review from its precedent, see Pet. App. 2a. To the extent petitioner believes that the court of appeals erred in relying on its precedent, he did not properly preserve that claim. To the extent that petitioner believes that the court of appeals simply misapplied that precedent in the unpublished decision below, that claim would not warrant this Court's intervention. See *Wisniewski* v. *United States*, 353 U.S. 901, 902 (1957) (per curiam).

In any event, petitioner does not identify any court of appeals that has applied a more exacting form of review to a criminal-fraud conviction than the decision below applied in this case. Nor does petitioner identify any sound basis for undertaking such review. Petitioner's reliance (Pet. 23-24) on decisions of this Court

reviewing certain non-fraud civil judgments for consistency with the First Amendment is misplaced. That practice does not compel the conclusion that a jury verdict of criminal fraud, which represents a finding of every element of the offense beyond a reasonable doubt, is subject to de novo review whenever the defendant claims that the statements found to be criminally fraudulent are worthy of First Amendment protection. Petitioner provides no sound reason why the procedures followed in this case—which included the normal safeguards of a criminal trial; a specific requirement of proof beyond a reasonable doubt of both knowledge of falsity and intent to defraud, Pet. App. 3a-4a; and "independent review" by the court of appeals, *id.* at 5a—were insufficient to protect any First Amendment rights that may be implicated in this case. See *Alvarez*, 132 S. Ct. at 2563 (plurality opinion); *Telemarketing Assocs.*, 538 U.S. at 620.[4]

Petitioner also overlooks that the application of the wire-fraud statute in this case is consistent with the government's broad authority to regulate misleading commercial speech. The statements at issue in this case did not appear in an academic scientific paper, but instead in a commercial press release aimed at boosting InterMune's sales and promoting its financial success. See, *e.g.*, Pet. App. 85a ("We believe these

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[4] Petitioner suggests (Pet. 21) that independent review is necessary in order to prevent the government from using fraud prosecutions as a tool for viewpoint discrimination. But aside from his baseless assertion that the criminal charges against him were motivated by a government effort to suppress scientific speech, he identifies no evidence that such viewpoint discrimination actually occurs in the enforcement of the viewpoint-neutral wire-fraud statute.

results will support use of Actimmune and lead to peak sales in the range of $400-$500 million per year, enabling us to achieve profitability in 2004 as planned."). The press release was targeted to potential customers (doctors, caregivers, patients, and their families), and sales representatives found it very effective in helping to convince doctors to prescribe Actimmune to IPF patients. Gov't C.A. Br. 11-12, 25. This Court has recognized that, as a general matter, "there can be no constitutional objection to the suppression of commercial messages that do not accurately inform the public about lawful activity." *Central Hudson Gas & Elec. Corp.* v. *Public Serv. Comm'n of New York*, 447 U.S. 557, 563 (1980).

Moreover, even assuming independent review of the sort petitioner apparently envisions were warranted, it would not change the outcome here. Even in the circumstances in which this Court undertakes an independent review, it is "an independent review *of the record*." *Bose Corp.* v. *Consumers Union of United States*, 466 U.S. 485, 505 (1984) (emphasis added). Such review would not allow petitioner or his amici to raise new arguments defending the accuracy of the press release for which petitioner did not lay an evidentiary foundation at trial. And for reasons already discussed, see pp. 17-18, *supra*, the actual record that was presented to the jury in this case does not support petitioner's theory that his statements were nonmisleading.

3. Petitioner finally contends (Pet. 27-31) that his conviction violated due process because he had "no notice that a reasonable * * * interpretation of accurate clinical study data constitutes wire fraud." As with petitioner's other arguments, this one likewise

rests on the erroneous premise that petitioner was convicted for his "scientific conclusions," Pet. 29, rather than for presenting the results of the drug trial in a misleading way. As previously explained, this case does not present a question about the regulation of scientific opinion.

Petitioner had sufficient notice that the conduct for which he was convicted was subject to criminal sanctions. The "touchstone" of vagueness analysis "is whether the statute, either standing alone or as construed, made it reasonably clear at the relevant time that the defendant's conduct was criminal." *United States* v. *Lanier*, 520 U.S. 259, 267 (1997). Petitioner accordingly can prevail only by showing that the statute failed to provide clear warning that his own conduct (rather than some other hypothetical conduct) was proscribed. *Holder* v. *Humanitarian Law Project*, 130 S. Ct. 2705, 2719 (2010). Here, petitioner's presentation of the study results in a misleading light falls squarely within the scope of the wire-fraud statute, which prohibits anyone who has "devised or intend[s] to devise any scheme or artifice to defraud" from making a wire transmission in interstate commerce "for the purpose of executing such scheme or artifice." 18 U.S.C. 1343. As the court of appeals correctly concluded, "[a]n ordinary person would have understood that if he made misleading statements in a press release with the specific intent to defraud he would be subject to the wire fraud statute." Pet. App. 6a (internal citation omitted). The district court, which directly heard all the evidence in this case, put it even more colorfully: "To contend that [petitioner] was not on notice that [he might face wire-fraud liability] if he lied in a press release about the success of [a]

clinical trial for a drug that might have sales as high as $500 million per year is simply ludicrous." *Id.* at 42a.

Although the wire-fraud statute does not, and could not, specifically enumerate every possible fraudulent scheme that a particular defendant might devise, petitioner had no reason to believe that his deliberately misleading press release would fall outside the statute's scope. Indeed, as previously mentioned, this Court has long held that "false and fraudulent representations may be made with respect to the curative effect of substances." *Seven Cases*, 239 U.S. at 517; see *Lanier*, 520 U.S. at 266 (noting that a "prior judicial decision" can provide notice of a statute's scope). It is also particularly significant that the statute includes an intent-to-defraud element, as this Court has "made clear that scienter requirements alleviate vagueness concerns." *Gonzales* v. *Carhart*, 550 U.S. 124, 149 (2007); see *Skilling* v. *United States*, 130 S. Ct. 2896, 2933 (2010); see also *United States* v. *Williams*, 553 U.S. 285, 306 (2008).

Petitioner's suggestion (Pet. 31-35), echoed by his amici, that the court of appeals' unpublished decision here will chill scientific debate is misconceived. Again, the court of appeals recognized that "genuine debates of any sort are, by definition, not fraudulent," and simply held that, on the facts of this case, petitioner fraudulently marketed a drug by presenting particular data in a particular misleading way. Pet. App. 6a. The efforts of petitioner and his amici to identify other instances of conduct that they think would be criminally prosecutable under the theory of this case overlooks the importance of examining each case individually, with a focus on the precise state-

ments made and the context in which they were presented. See, *e.g.*, *Matrixx*, 131 S. Ct. at 1321. Here, the government presented contextual evidence that established beyond a reasonable doubt that petitioner's statements were misleading and calculated to have that precise effect. If counter-evidence existed that could have rebutted that showing, petitioner did not present it to the jury. He cannot now make such a factual showing in appellate briefs based on self-selected materials that the jury never considered and that the government had no opportunity to refute. No basis exists for this Court's review.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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NOVEMBER 2013