
# Preventative Medicine for Biotech Boards: Lessons Learned from Life Sciences Securities Litigation

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May 14, 2021

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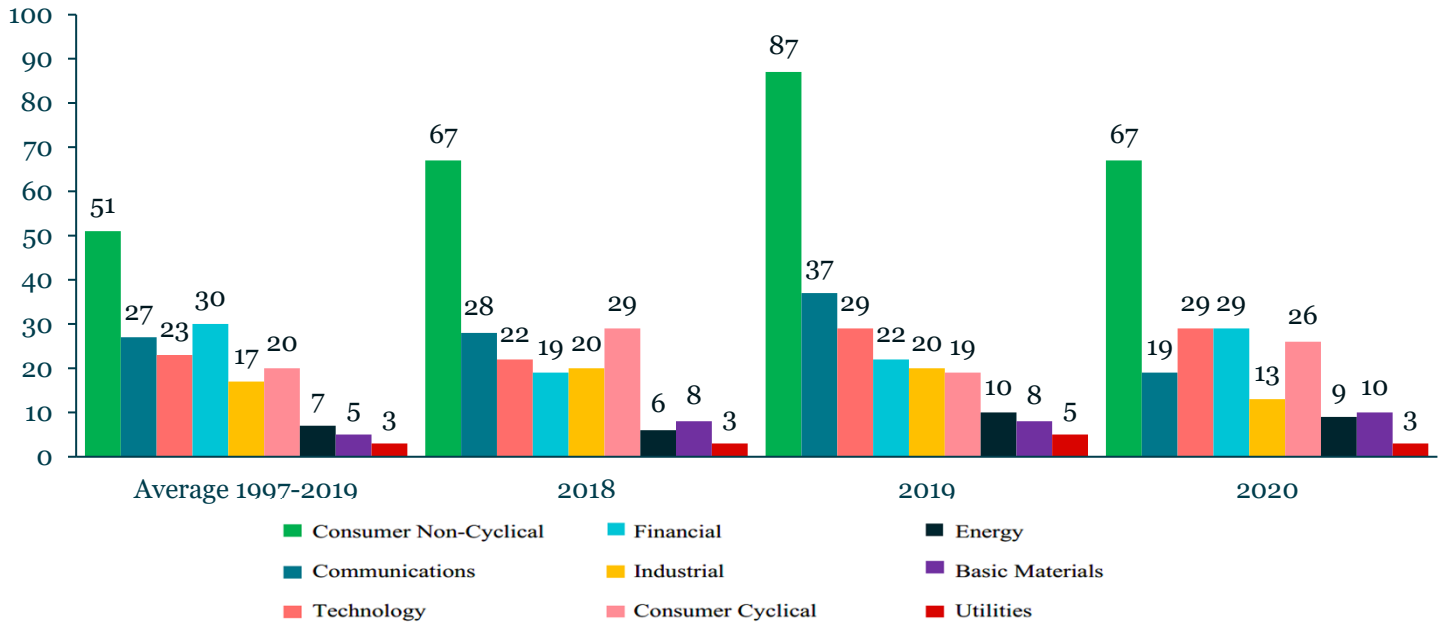
# Agenda

- Securities Class Action Landscape for Biotechnology Companies
  - The Rising Tide of Lawsuits Against Biotech Companies
  - Trials and Tribulations of Biotech Companies: Why Are They Such Popular Targets for Plaintiffs?
- Preventative Medicine:
  - The Dilemma of Interim Data and Ongoing Trials
  - Disclosing Interim FDA Communications
  - Disclosure of Form 483s

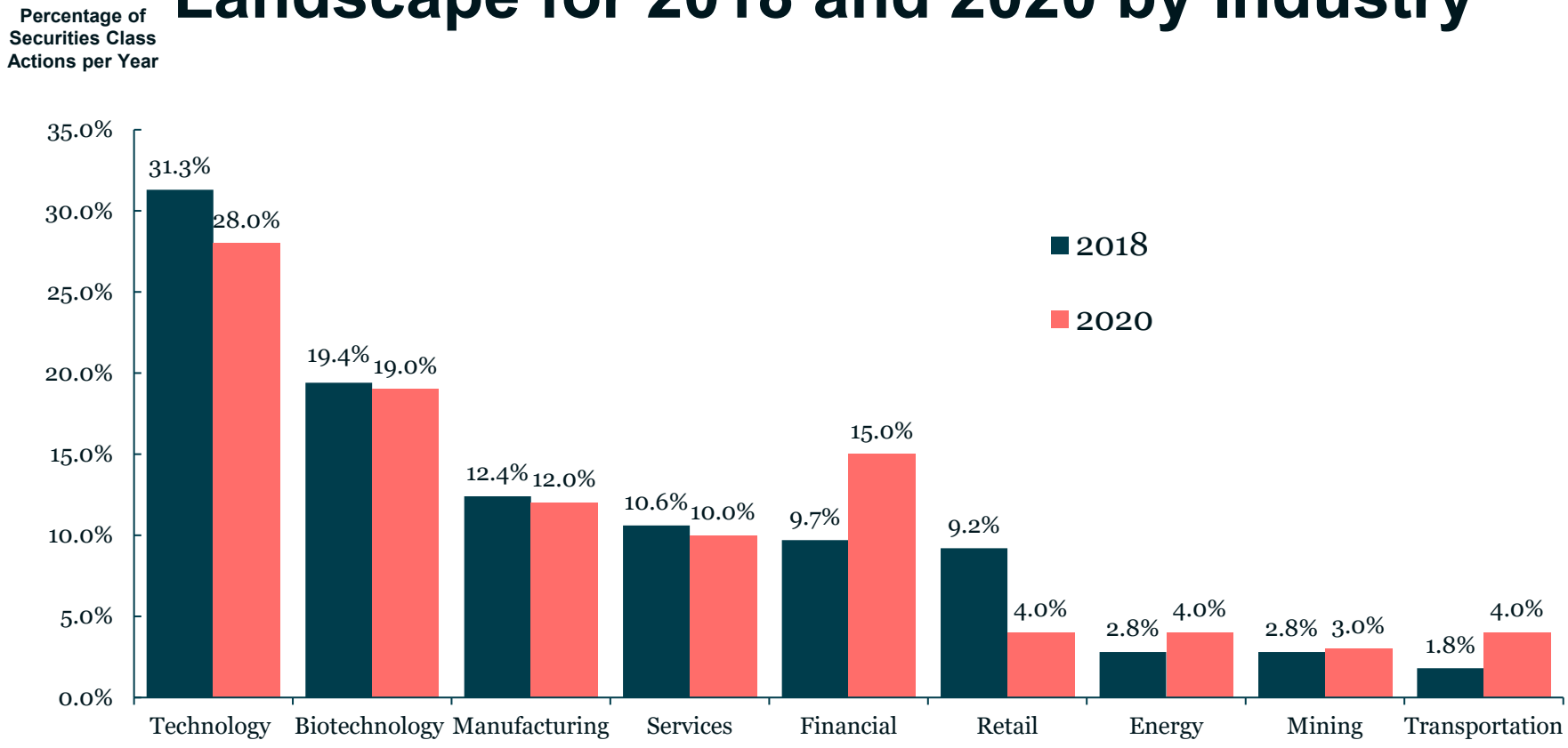
# Filings by Industry—Core Federal Filings




Note: Consumer Non-Cyclical is primarily composed of pharmaceutical, healthcare, and biotechnology firms

Source: Cornerstone Research: Securities Class Action Filings—2020 Year in Review

# The Securities Class Action Landscape for 2018 and 2020 by Industry






Source: Woodruff Sawyer Securities Class Action Insights

# The Trials and Tribulations of Clinical Trials

- Tapping public markets with high valuations at early stages of development
  - Betting big on a hypothesis
- Investors' voracious appetite for information
  - Often prompts premature disclosures
- Data is often preliminary and can change/reverse
  - Interim results are not conclusive
- FDA approval process is iterative, ongoing, and subject to change
  - After-the-fact publication of briefing documents
- Binary outcomes lead to one-day double-digit drops
  - Clinical trial success or failure
  - FDA approval and compliance

# Preventative Medicine: The Dilemma of Interim Data and Ongoing Trials

- Dissemination of topline results does not trigger duty to disclose full results
- “Half-truths” regarding results can lead to liability
  - Omissions of data that create a more favorable impression regarding results
- Disclosure of positive interim data:
  - May be misleading if not accompanied by sufficient warning that interim results have a high degree of uncertainty
  - May be misleading if subsequent results in ongoing trial are inconsistent or less favorable
    - Dilemma of disclosing data “as of” a certain prior date
    - Particularly problematic in open label trials
- Continued discussion of data from earlier completed trials:
  - May be misleading when interim results from subsequent trials are inconsistent or less favorable

# The Dilemma of Interim Data and Ongoing Trials: Case Study

*Roche* (D.N.J. 2018)

- Reports topline results of Phase 3 trial for treatment pairing Herceptin with a newer drug and states complete results will be provided at ASCO:
  - Study met its primary endpoint, showed statistically significant improvement in invasive disease-free survival (iDFS), and demonstrated safety profile consistent with that seen in earlier trials
  - Describes results as "positive"
- Expresses confidence that Herceptin franchise would survive introduction of biosimilars and stated result was "terrific news" for patients
- Investors react negatively to disclosure of full results at ASCO:
  - Improvement in iDFS is 19%, the p-value within only a "hair" of statistical significance improvement is attributable to one subgroup, and the drug substantially increases safety risks in three areas

# Polling Question #1

- Did the court find that plaintiffs adequately alleged:
  - That Roche's statements about topline results from its Phase 3 trial were misleading?
  - That Roche's characterization of results as "positive" and its statements about the Herceptin franchise were misleading?

- District Court granted Motion to Dismiss
  - Roche was not responsible for market's belief that "positive" outcome required 20% improvement; safety risks, though high, were in line with data in previous study; and there was no obligation to disclose that improvement was attributable to a single subgroup
  - Statements regarding "positive" results, "terrific news," and Herceptin franchise were non-actionable opinions and puffery

# The Dilemma of Interim Data and Ongoing Trials: Case Study

*Clovis* (D. Colo. 2017)

- Developing lung cancer drug: its Phase 1/2 trials measured tumors for shrinkage at various points along a multi-cycle timeline
  - Trial protocol required that the ORR yielded by an initial scan be confirmed through follow-up tumor scans
- Tells investors that ORRs are between 50-60% for 9 months
- Announces previously reported ORR data was based on mixture of unconfirmed and confirmed response and that confirmed ORRs were as low as 28%
- Subsequent safety data showed severe cardiac events and NDA is withdrawn
- Plaintiffs sue, alleging that at the time company reported ORRs of 50-60%, follow-up scans had already undermined the original favorable responses
- District Court denied Motion to Dismiss
  - Rejected argument that protocol did not require updating initial ORRs as soon as new data from follow-up screens became available
  - Credited plaintiffs' motive argument: company acted in the hope that negative results from early follow-up scans would subsequently be overtaken by positive results from later scans

# Preventative Medicine: FDA Communications

- No duty to disclose interim negative feedback
  - Courts recognize there is a give and take with FDA
- General optimism about approval withstands challenge even in the face of some undisclosed negative interim FDA feedback
  - Robust risk factors key
- Dangers
  - Characterizing FDA's comments: Let the minutes speak for themselves
  - Expressing optimism about a particular topic while failing to disclose FDA concerns on that topic
    - Can't say you believe tumors won't translate into humans when FDA already raised concerns about human carcinogenicity
    - Can't say you are optimistic about FDA approval when FDA has recommended a second trial before submitting NDA

# FDA Communications: Case Study

*Sarepta* (2018)

- Company discloses that it plans to gather additional data before filing NDA because FDA had expressed skepticism about biopsy data
- FDA subsequently requests independent review of biopsy results
- Company reiterates belief that existing data could support accelerated review without disclosing FDA request
- Company subsequently announces delay in filing NDA because FDA is requiring additional and reassessed data
- Stock drops 32%; investors sue

# Polling Question #2

- Did the court find that plaintiffs adequately alleged that Sarepta's statements concerning the availability of accelerated review were misleading?

- First Circuit affirms lower court's order dismissing case:
  - No duty to disclose agency communications that were simply part of an "interim regulatory back and forth"
  - FDA had not told Company that compliance with its request for independent lab analysis was mandatory
  - Company had robust disclosures regarding accelerated FDA approval

# FDA Communications: Case Study

*Esperion Therapeutics* (2018)

- After end-of-Phase 2 meeting with FDA, Company tells investors that FDA would accept use of surrogate endpoints (lowering of cholesterol) and not require a pre-approval cardiovascular outcomes trial ("CVOT")
- In subsequent press release, Company warns: "Esperion may need to change the design of its Phase 3 program once final minutes from the FDA meeting are received"
- FDA minutes released a month later: indicate FDA had encouraged Company to commence a CVOT promptly because any concerns in such trial could require that a full CVOT trial be completed prior to approval
  - Stock drops; investors sue
- Sixth Circuit reverses lower court's order dismissing case:
  - Distinguished cases where FDA interim guidance was less definitive and not inconsistent with Company's statements to investors
  - Noted that Company failed to challenge minutes under FDA appeal process

# Preventative Medicine: Disclosure of FDA Form 483s

- Disclosure required only if material and if omission renders a statement misleading
- Materiality depends on context in which Form 483 is issued
  - Courts recognize Form 483s are “observational in nature” and not final findings
- Ordinarily not material if issued as part of regular inspection cycle of global manufacturers and observations are believed to be remediable
- May be material in context of:
  - Failed re-inspection leading to severe regulatory sanctions; or
  - Failed inspection required for approval of new drug critical to Company’s success
- Statements rendered misleading by non-disclosure of Form 483
  - Claims of CGMP compliance/corrective actions substantially complete
  - Warnings that receipt of Form 483 is “potential” risk

# Form 483s: Case Study

*Nabriva Therapeutics* (S.D.N.Y. 2020)

- Company had no revenues and only two products under development
- Files NDA for drug to treat complicated urinary tract infections in Oct. 2018
- FDA inspects contract manufacturer and issues Form 483 listing 10 observations in Dec. 2018
- States that FDA had not identified any potential review issues in connection with NDA in Jan. 2019 and spoke optimistically about FDA approval
- 10-K identifies as risk factor reliance on a third-party manufacturer and possibility of warning letter and regulatory action if manufacturing problems arise
- Announces that FDA denied NDA based on manufacturing deficiencies

# Polling Question #3

- Did the court find that plaintiffs adequately alleged that Nabriva's "no potential review issue" statement was misleading?

- District Court rejects per se rule regarding materiality of Form 483
  - Given breadth of Form 483, plaintiffs sufficiently alleged falsity of "no potential review issue" statement and risk disclosure
  - Optimistic statements re: FDA approval not actionable since observations could have been remedied
  - Dismissed on scienter grounds

# Form 483s: Case Study

*Immunomedics* (D.N.J. 2020)

- Developing biologic for treatment of metastatic triple negative breast cancer
- Discovers data integrity breach at manufacturing plant and reports breach to FDA
- Submits BLA for biologic, followed by $300 million stock offering
- Makes optimistic statements regarding FDA approval process
- FDA conducts pre-approval manufacturing facility inspection and issues Form 483
- SEC filings contain risk disclosures regarding potential data breaches and potential receipt of Form 483s
- Details of Form 483 disclosed by third parties (FDANews and an analyst)
- FDA issues a Complete Response Letter
- District Court denies Motion to Dismiss
  - Plaintiffs sufficiently alleged falsity of optimistic statements re: approval process and risk disclosures
  - Plaintiffs adequately alleged scienter: defendants knew about data integrity breach and conducted secondary offering while BLA was pending but before disclosure of data breach

# Key Takeaways

- Considerable litigation risk from failed clinical trials and FDA non-approvals
- Simple steps you take now can make a future case more defensible
  - Plan prophylactically; prevention is the best medicine
- Exercise special caution in:
  - Reporting preliminary results in an ongoing trial
  - Discussing favorable results from earlier completed trials during a later ongoing trial
  - Characterizing FDA communications
- Review statements re: CGMP compliance and risk factors re: FDA inspections upon receipt of Form 483s
- Well-crafted risk factors and couching optimistic statements as opinions (e.g., “we believe. . .”) can aid in the defense of claims

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# Presenters

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