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HOW AND WHEN TO TELL YOUR STORY: PUBLIC DISCLOSURES BY LISTED LIFE SCIENCES COMPANIES

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September 28, 2021

PUBLIC DISCLOSURES AS A WINDOW INTO THE INDUSTRY AND BUSINESS

General Themes

- What to disclose and when
- Addressing clinical, regulatory, and IP developments
- Crafting risk factors
- Dealing with surprises
- Case studies

Disclosure Obligations

- Public companies must (periodically) disclose material information to their investors
- What to disclose and when?
- What is material?
- Need to provide nuanced disclosure to give meaningful information
- Often incomplete – which could be misleading
  - Partial or preliminary data (“top line” results) or regulatory input
  - Serious adverse events without confirmatory data

When to Disclose

- Periodic reporting
- Regular news flow
- “Data inflection points”
- Scientific conferences
- Unforeseeable events

Dynamics of the Industry and Business

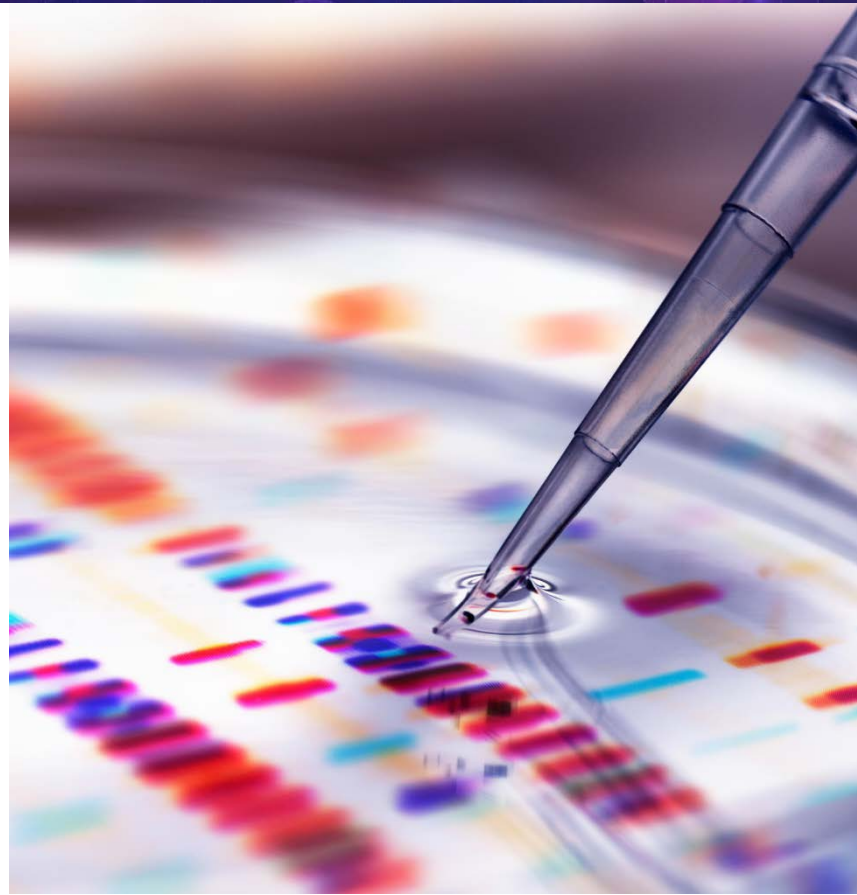
- Biotech companies don’t have (much) revenue
- Financial results are largely irrelevant
- “Cash runway” – aligned with development plan – is key financial metric
- (Almost) all value is in the future, driven by:
  - Science
  - Clinical results
  - Regulatory approvals
  - IP protection and FTO
  - Partnerships
  - Competitive therapies
  - Luck

What Drives Value, Up or Down

- Data
- Regulatory news
- IP developments
- Collaborations/licensing/partnerships
- Competitors
- Surprises

Goal

- Demonstrating safety and efficacy
  - On time
  - On budget
  - In accordance with trial protocol
- May be entirely dependent on a single product candidate in development



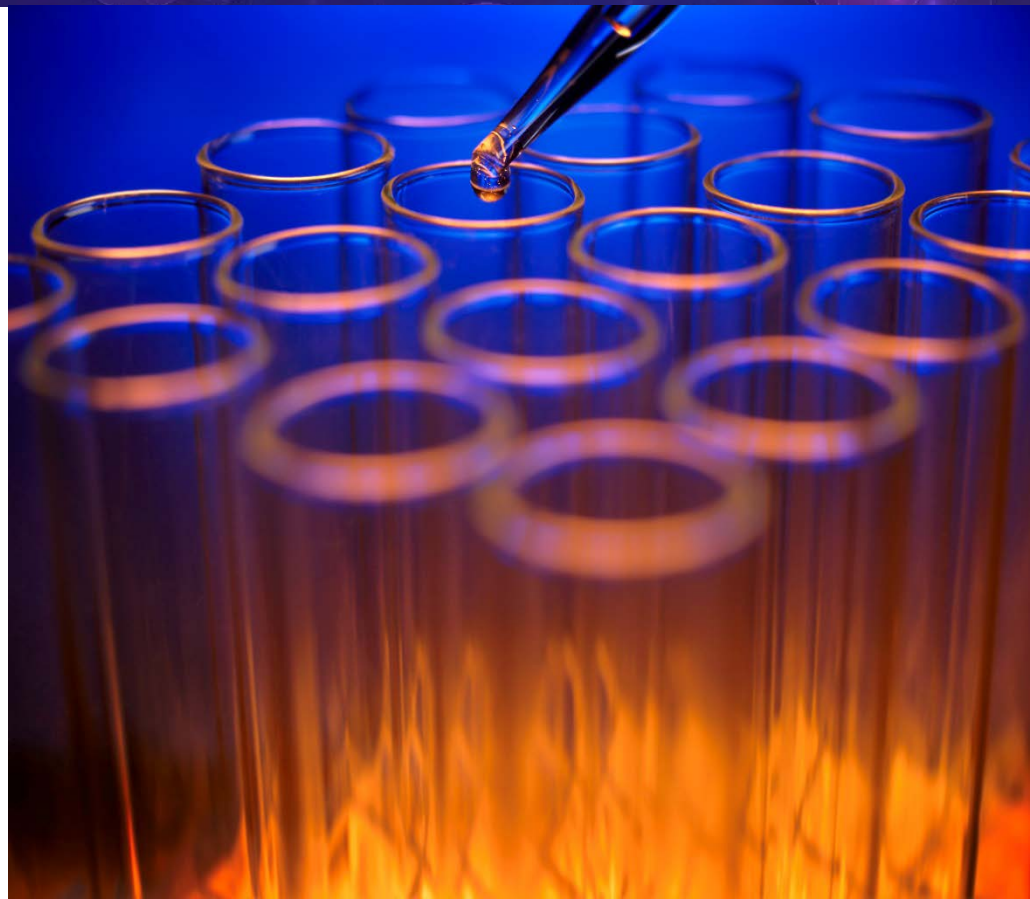
Giving “Guidance” to the Market

- When data will be reported
- When approvals will be obtained
- When cash will run out

    - *Biggest risk: (too much) hope/faith*

Specific Challenges

- Early-stage vs late-stage trials
- Top-line data
- Open label trials
- Enrolment curve
- Informal regulatory advice
- IP developments
- Cherry picking
- Disclosure may be “literally true”, but still misleading



Potential Problems

- SEC investigations
- FDA concerns
- Stockholder litigation

- SEC and FDA talk to one another

FDA Issues

Life sciences industry is highly regulated and subject to a number of different and changing laws and standards, of which investors need to be made aware

- Depending on the product—FDA, EMA, CDC, NIH, USDA, NRC, etc., etc.
- What happens when the law or standards change mid-game and how detailed do we need to get?
  - Laws, regulations, guidance documents
  - Agency precedent

FDA Issues (continued)

Many issues / events can come up during the life of a development program, including, but not limited to:

- FDA comments/advice
- Failure to obtain anticipated designations
- Adverse study results
  - Safety (1 adverse event v. a trend)
  - Efficacy
  - Does the population and study phase matter?--YES
- Changes to development plants (e.g., interim analyses)
- Early-stage results that are positive but not statistically significant
- Results on secondary endpoints

FDA Issues (continued)

Many issues / events can come up during the life of a development program, including, but not limited to:

- Interim results
- Continuous results
- Clinical trials that do not proceed as planned
- Study monitoring results
- Manufacturing issues

When something happens (and it invariably does), how much detail is needed?

IP Issues

Evolving global IP landscape

- Laws are not stagnant – developing law around the globe can wreak havoc on current scope of intellectual property protection
  - Brazil just recently adjusted its patent term from the later of 10 years from issuance or 20 years from first filing to simply 20 years from first filing.
    - Effected the patent term of thousands of already issued patents
  - Patentability requirements for bio/pharma inventions in the US are being tightened
    - Written description and enablement (see, *Ariad*, *AbbVie*, *Amgen*, *Idenix*, *Juno*)

IP Issues (continued)

Ownership interests in intellectual property

- Government funding may complicate ownership
  - NIH contributed $$$ to Moderna's COVID vaccine and may have a stake in its patents
    - Government could license or otherwise control price
- Timely recordation of patent rights as a means to avoid loss of rights to subsequent purchaser
  - Representations that a company owns a patent where it has not yet been assigned could be problematic
    - Use employment contracts to affirmatively state that the employee is under an obligation to assign the invention to the employer

IP Issues (continued)

Ongoing patent surveillance

- Challenges may be made to patents after issuance affecting the scope of rights
  - IPRs, oppositions, etc.
- New competitor patents identified by ongoing patent prosecution and FTOs
- Surveillance for potential infringers
  - Lack of vigilance can provide laches defense

Crafting Risk Factors

Really only need one:

- “We are a biotech company and you may lose all of your money.”

General approach:

- An insurance policy: best to be negative
- Specific, concrete, relevant
- Even within this approach, there are varying degrees of detail and specificity

Risk Factors

- Clinical development challenges
- Regulatory status
- IP issues: FTO problems; challenges to own IP; IP licenses
- Cash burn; raising money
- Corporate development: partnering, licensing, collaboration
- Competition, market, pricing
- Manufacturing challenges: process validation

Crafting Risk Factors – a sampling

- The timing, progress, and results of our preclinical studies and clinical trials for our product candidates
- The timing, scope or likelihood of regulatory filings and approvals for our product candidates
- Our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, claims others may make regarding rights in our intellectual property, and any potential infringement, misappropriation or other violation of any third-party intellectual property rights
- Our ability to successfully commercialize any product candidate for which we receive regulatory approval and our expectations regarding the size of the patient populations or the market acceptance of our product candidates if approved for commercial use
- Our ability to compete with other biopharmaceutical, biotechnology companies and other third parties and risks associated with such third parties developing or commercializing products more quickly or marketing them more successfully than us

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

Clinical and non-clinical development is expensive, time-consuming, and uncertain as to outcome. Our product candidates are in different stages of clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs.... Events that may prevent successful or timely completion of clinical development, as well as product candidate approval, include, but are not limited to:

- Occurrence of **serious adverse events** associated with a product candidate that are viewed to outweigh its potential benefits;
- Delays or failure in reaching a consensus with regulatory agencies on **study design**;
- Delays in reaching agreement on acceptable terms with prospective clinical research organizations ("CROs") and clinical trial sites;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Delays in receiving regulatory authorization to conduct the clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- Delays in obtaining or failure to obtain required IRB and IBC approval at each clinical trial site;
- Requirements of regulatory authorities, IRBs, or IBCs to modify a study in such a way that it makes the study impracticable to conduct;
- Regulatory authority requirements to perform additional or unanticipated clinical trials;
- Regulatory authority refusal to accept data from foreign clinical study sites;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Disagreements with regulatory authorities regarding our study design, including endpoints, our chosen indication, or our interpretation of data from preclinical studies and clinical trials or a finding that a product candidate's benefits do not outweigh its safety risks;
- Imposition of a **clinical hold** by regulatory agencies after an inspection of our clinical trial operations or trial sites;
- Suspension or termination of clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics (alone or in combination with other products) of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Failure by CROs, other third parties or us to adhere to clinical trial requirements or otherwise properly manage the clinical trial process, including meeting applicable timelines, properly documenting case files, including the retention of proper case files, and properly monitoring and auditing clinical sites;
- Failure of sites or clinical investigators to perform in accordance with Good Clinical Practice or applicable regulatory guidelines in other countries;
- Failure of patients to abide by clinical trial requirements;
- Difficulty or delays in **patient recruiting** into clinical trials or in the addition of new investigators;
- The impact of the COVID-19 pandemic on the healthcare system or any clinical trial sites;
- Delays or deviations in the testing, validation, manufacturing, and delivery of our product candidates to the clinical sites;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Delays in having patients complete participation in a study or return for post-treatment follow-up;
- The number of patients required for clinical trials of our product candidates being larger than we anticipate;
- Clinical trials producing negative or inconclusive results, or our studies failing to reach the necessary level of statistical significance, requiring that we conduct additional clinical trials or abandon product development programs;
- Interruptions in manufacturing clinical supply of our product candidates or issues with manufacturing product candidates that meet the necessary quality requirements;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Unanticipated clinical trial costs or insufficient funding, including to pay substantial application user fees;
- Occurrence of **serious adverse events** or other undesirable side effects associated with a product candidate that are viewed to outweigh its potential benefits; or
- **Changes in regulatory requirements** and guidance, as well as new, revised, postponed, or frozen regulatory requirements, ... that require amending or submitting new clinical protocols, undertaking additional new tests or analyses, or submitting new types or amounts of clinical data.

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for approval or if there are safety concerns or adverse events associated with our product candidates, we may:

- Be delayed in or altogether prevented from obtaining marketing approval for our product candidates;
- Obtain approval for indications or patient populations that are not as broad as intended or desired;

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates

- Obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- Be subject to changes with the way the product is administered;
- Be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- Be subject to the addition of labeling statements, such as warnings or contraindications;
- Be sued; or
- Experience damage to our reputation.

Risks Related to Intellectual Property

If we are unable to obtain, maintain and protect our intellectual property rights for our technology and product candidates, or if our intellectual property rights are inadequate, our competitive position could be harmed.

...The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation and subject to change with regulatory agencies and court decisions. As a result, the issuance, scope, validity, enforceability and commercial value of our licensed patents and any patents we own in the future are highly uncertain. The steps we have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information, use by third parties of our products or infringement of our intellectual property rights, both inside and outside of the United States....

Risks Related to Intellectual Property

Third parties may in the future initiate legal proceedings alleging that we are infringing their intellectual property rights, and we may become involved in lawsuits or other administrative procedures to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful and have a material adverse effect on the success of our business.

... The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any other future product candidates. Third parties may assert infringement or other intellectual property claims against us based on existing patents or patents that may be filed and/or granted in the future. At times we may attempt to initiate litigation or other administrative procedures to invalidate or otherwise limit the scope of a third party's intellectual property and these attempts may not be successful. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such intellectual property rights are invalid, unenforceable or otherwise not infringed, we could be required to obtain a license from such third-party to continue developing, manufacturing and commercializing our product candidates....

Case Study A

- Company A is developing a gene therapy to treat Indication A, which is in Phase 3 trials.
- One patient on trial has been diagnosed with a rare cancer (a “serious adverse event”). The patient had numerous unrelated risk factors for cancer. It is unclear whether the cancer was caused by, or related to, treatment
  - The company reports the SAE to the FDA. A few days later, the FDA imposes a “clinical hold”, requiring that dosing of patients be stopped
  - The company is conducting various tests and analyses, with the hope that they will demonstrate that the cancer was unrelated to the product candidate, for submission to the FDA. Various people in the company, including in management, will see those results developing as that process unfolds. If FDA accepts the outcome, they would lift the clinical hold, and the trial could proceed

Case Study A (continued)

- Per the protocol, the Company conducts an interim analysis. Based on the interim analysis, the Company increases the size of the trial.
- The Company applies for breakthrough drug designation. FDA does not grant the designation.
  - The Company previously announced that it would be applying for breakthrough designation
  - What if the Company did not announce the application?
- The Company goes in for a meeting with FDA.

Case Study B

- Company B is developing a therapy for the treatment of Indication B. The clinical trial protocol provides for enrolment of 150 patients
- The company has guided the market to full enrolment in the trial by October 2021, initial interim top-line data by March 2022, and full dataset by October 2023
- The company has also guided the market to “cash out” in H2 2024
- Internally, the company has budgeted for the enrolment of 30 patients per month for five months
- The client has enrolled 16 patients in month 1, and 12 patients in month 2

CLE Credit

RO78TZ5

*For those seeking CLE credit, the code is **RO78TZ5**.*

Kindly insert this code in the pop-up survey appearing at the end of this program.

Questions?

Biography

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Jacqueline R. Berman advises companies on US Food and Drug Administration (FDA) regulatory, compliance, and enforcement issues, as well as clinical trials and FDA-regulated product development programs. She also counsels clients on the safety, labeling, and reporting requirements for consumer products under the laws enforced by the US Consumer Product Safety Commission (CPSC), the Federal Trade Commission (FTC), and related state enforcement agencies. Jacqueline's clients include pharmaceutical, device, biologic, dietary supplement, and food/food additive manufacturers.

Biography

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A registered patent lawyer, Christopher J. Betti, Ph.D., concentrates his practice on biotechnology and pharmaceutical patent matters with an emphasis on biologics-related patent prosecution and patent litigation. Christopher also devotes a significant portion of his practice to product life-cycle management, intellectual property portfolio management, pre-litigation counseling, due diligence analysis associated with venture capital financing and public offerings, and opinions and strategic advice relating to complex patentability, patent validity, infringement, and freedom-to-operate issues.

Biography

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With more than 20 years of international experience in life sciences, Tim Corbett advises clients on complex cross-border corporate transactions, including public and private equity and debt offerings, mergers and acquisitions (M&A), joint ventures (JVs), and venture capital financings, including representations of both companies and investors. Tim also assists public and private clients with day-to-day corporate matters, including governance, securities law compliance, and disclosure requirements and practices.

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Latin America
Middle East
North America

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