Revolutionizing Medicine: The Race to Unlock the Power of Gene Therapy and Build a Competitive Edge

Sheena X. Wang

Aydin H. Harston

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- What is Gene Therapy
- The CRISPR/Cas System
- Patent Landscape and Considerations

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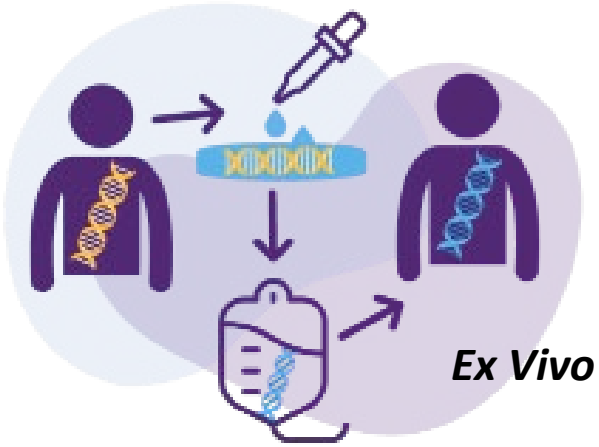
What is Gene Editing?

What is Gene Therapy?

- Techniques that modify a person's genes to treat or cure a disease.
- Gene therapy products have been approved or are being developed to treat diseases such as cancer, genetic diseases, and infectious diseases.

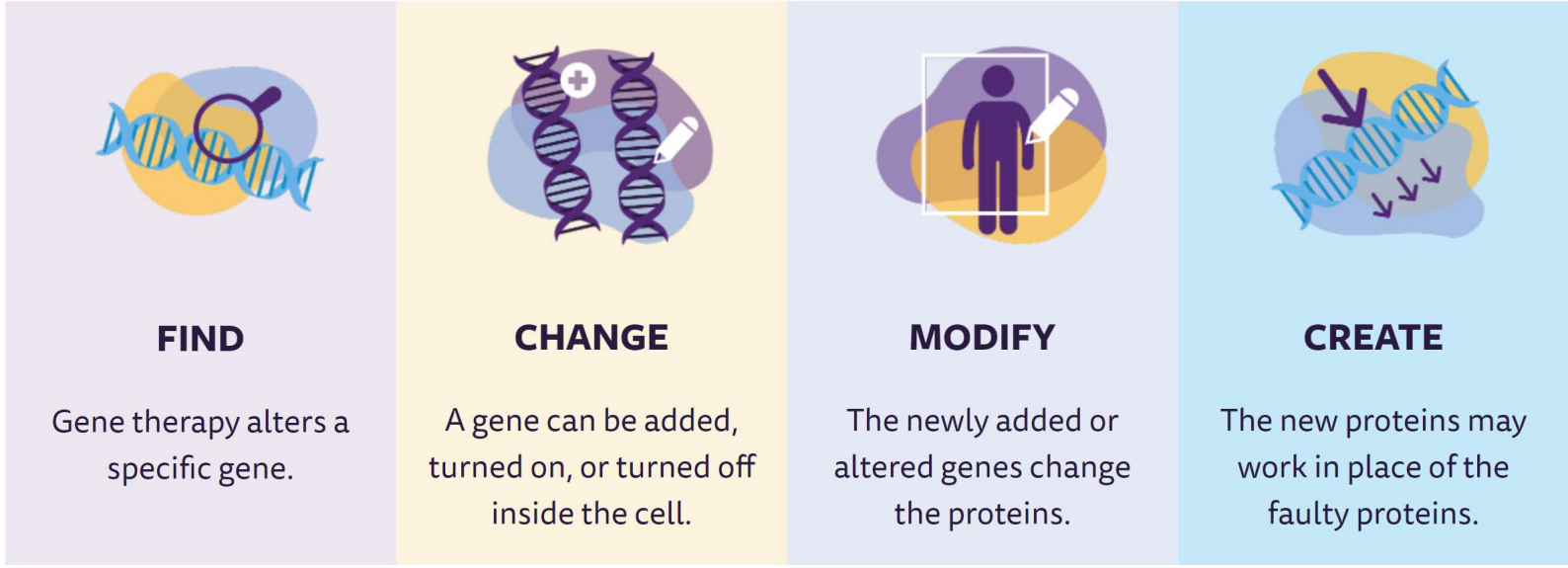


Source: What is Gene Therapy?, U.S. FDA (Jul. 25, 2018), https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy; GENE POSSIBILITIES, https://www.genepossibilities.com/how-does-gene-therapy-work(Last visited Jun. 19, 2023)

What is Gene Therapy?

Gene therapies can work by several mechanisms:

- Genome Editing: Replacing a disease-causing gene with a healthy copy of that gene (ex. CRISPR)
- Regulatory Oligonucleotides: Inactivating a disease-causing gene (ex. siRNA)
- Gene Addition: Introducing a new gene into the body to help treat a disease (ex. viral vector/LNP delivered gene therapies)



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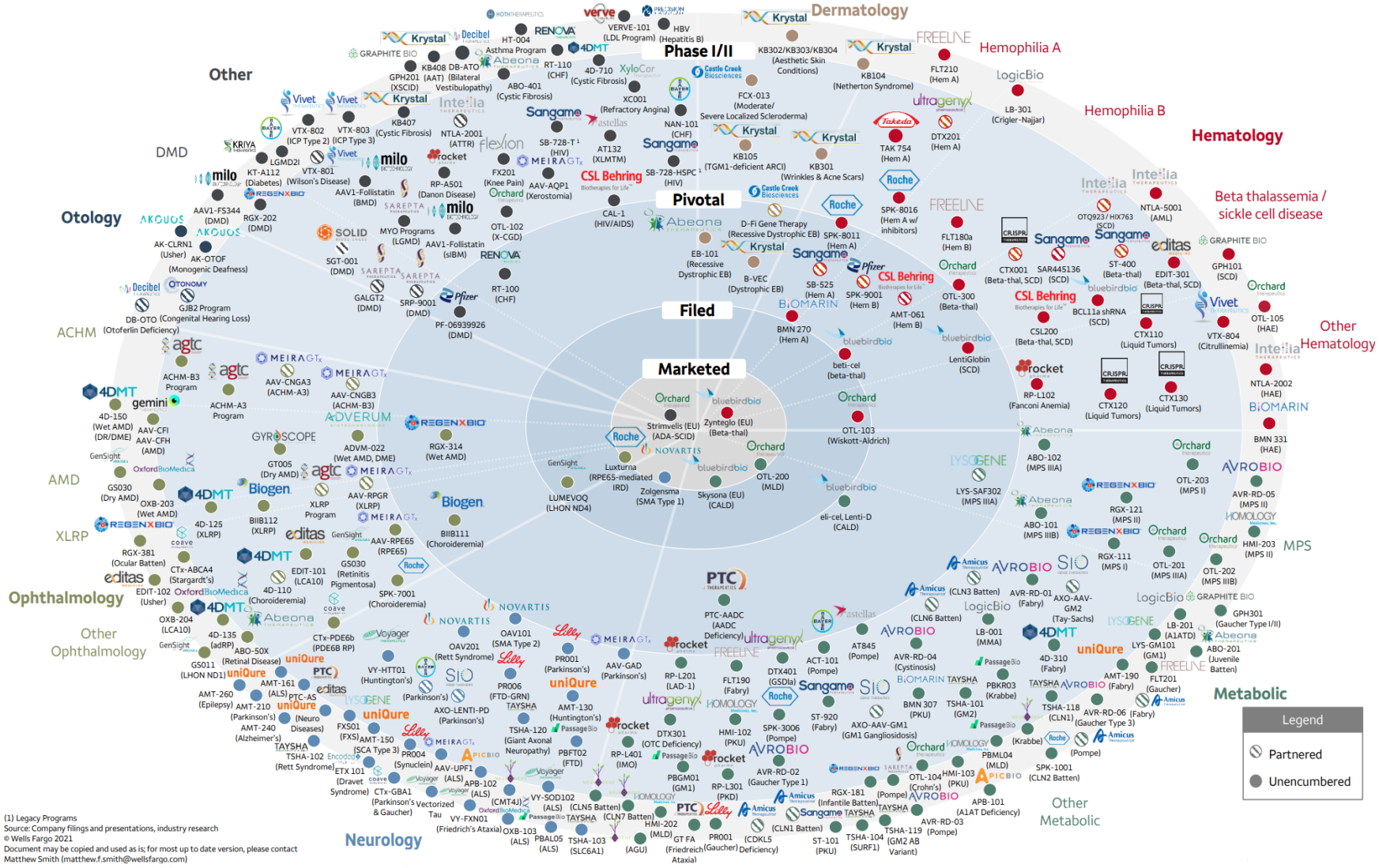
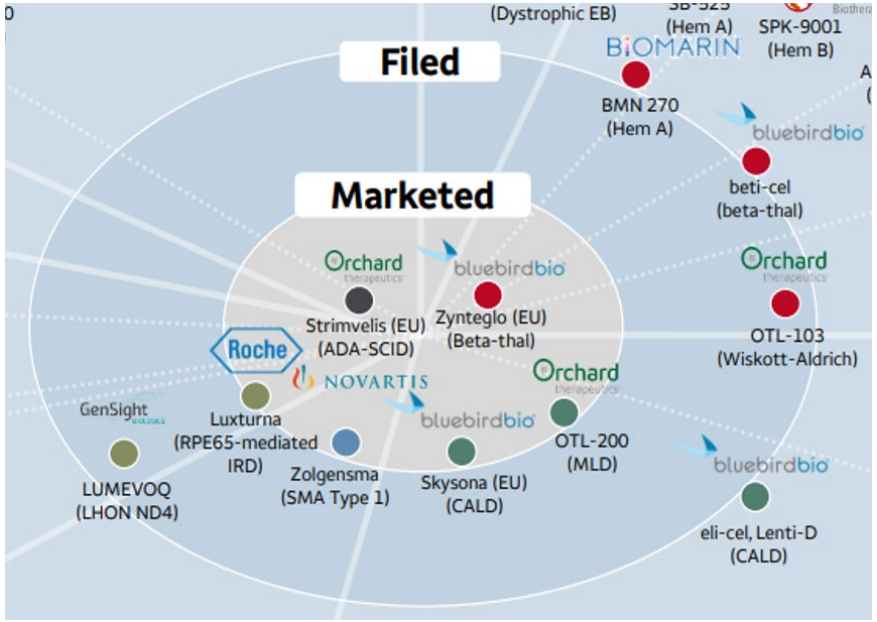
Many Players in the Gene Therapy Arena



Source: Wells Fargo Legacy Programs, 2021

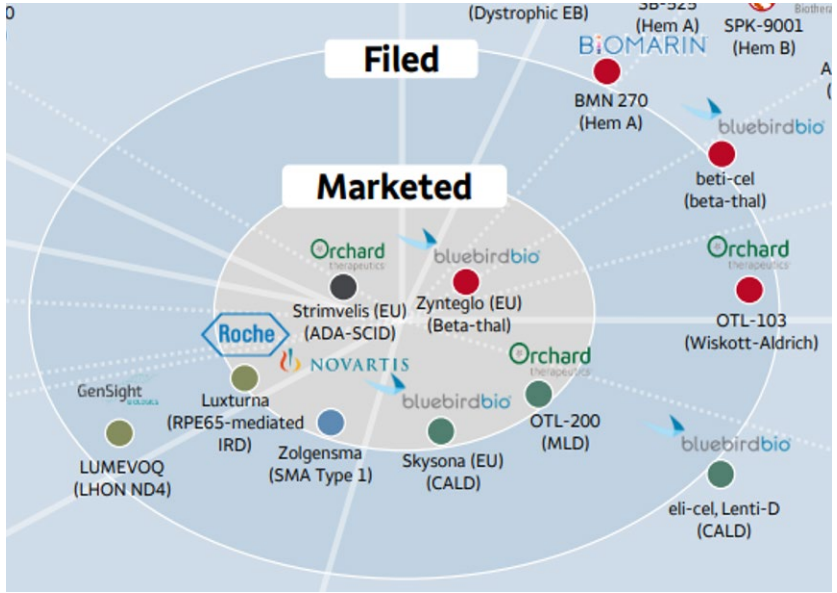
Players in the Gene Therapy Arena



- Orchard Therapeutics
  - Market Cap = $93.236M
  - Number of Employees = 259
  - Strimvelis® is a an *ex vivo* gene therapy approved by the European Medicines Agency (EMA) in 2016.
  - OTL-200/Libmeldy is an *ex vivo* gene therapy was approved by the EMA in 2020.
- Bluebird Bio
  - Market Cap = $405.43M
  - Number of Employees = 518
  - Zynteglo® is a an *ex vivo* gene therapy approved by the FDA in 2022.
  - Skysona® is a an *ex vivo* gene therapy approved by the FDA in 2022.

Source: Wells Fargo Legacy Programs, 2021 and Google Finance

Players in the Gene Therapy Arena



- Novartis
  - Market Cap = $225.50B
  - Number of Employees = 103,000
  - Zolgensma® viral vector gene therapy approved by the FDA in 2019.
- Roche
  - Market Cap = $253.05B
  - Number of Employees = 103,613
  - Luxturna viral vector gene therapy approved by the FDA in 2022.
- Gensight Biologics
  - Market Cap = € 34.20M
  - Number of Employees = 45
  - Lumevoq a viral vector gene therapy. GenSight withdrew its EMA application in April 2023 based on the EMA's Committee for Advance Therapies (CAT)'s indication that its current data is not sufficient to support market approval.

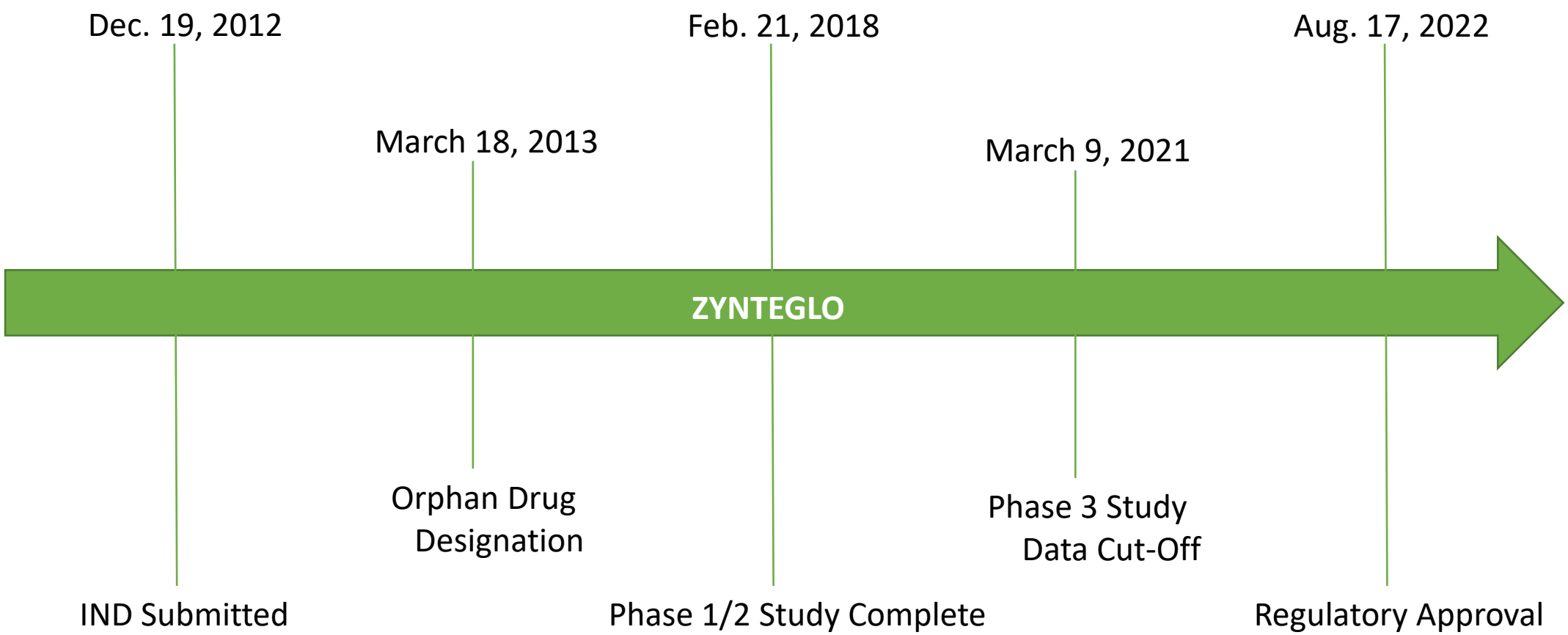
Source: Wells Fargo Legacy Programs, 2021 and Google Finance

Exemplary Gene Therapy: zynteglo

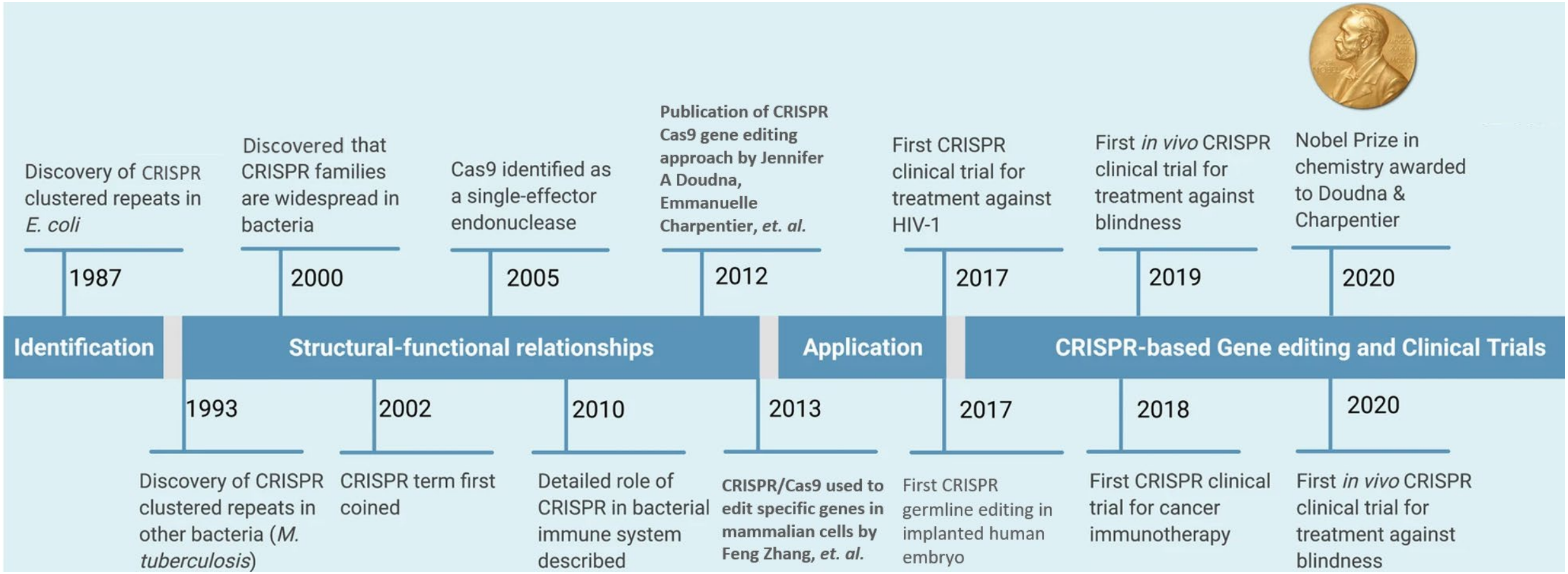
- A treatment for transfusion-dependent beta thalassemia, a disease that in severe cases requires regular blood transfusions for life.
- Developed by BlueBird Bio Inc. over approximately 10 years.
- Approved on August 17, 2022.
- Cost $2.8 million per patient.
- The drug is a type of cell therapy, it works by adding normal copies of the modified β-globin gene to the patient's own CD34+ cells *ex vivo* using lentiglobin viral vector BB305.
- Safety concerns, while no cases of cancer were reported in studies of Zynteglo, the FDA is concerned about potential risks.

Source: *ZYNTEGLO*, **U.S. FDA** (Sep. 19, 2022); *ZYNTEGLO*, **EUROPEAN MEDS. AGENCY** (last visited Jun. 14, 2023).

Exemplary Gene Therapy: zynteglo



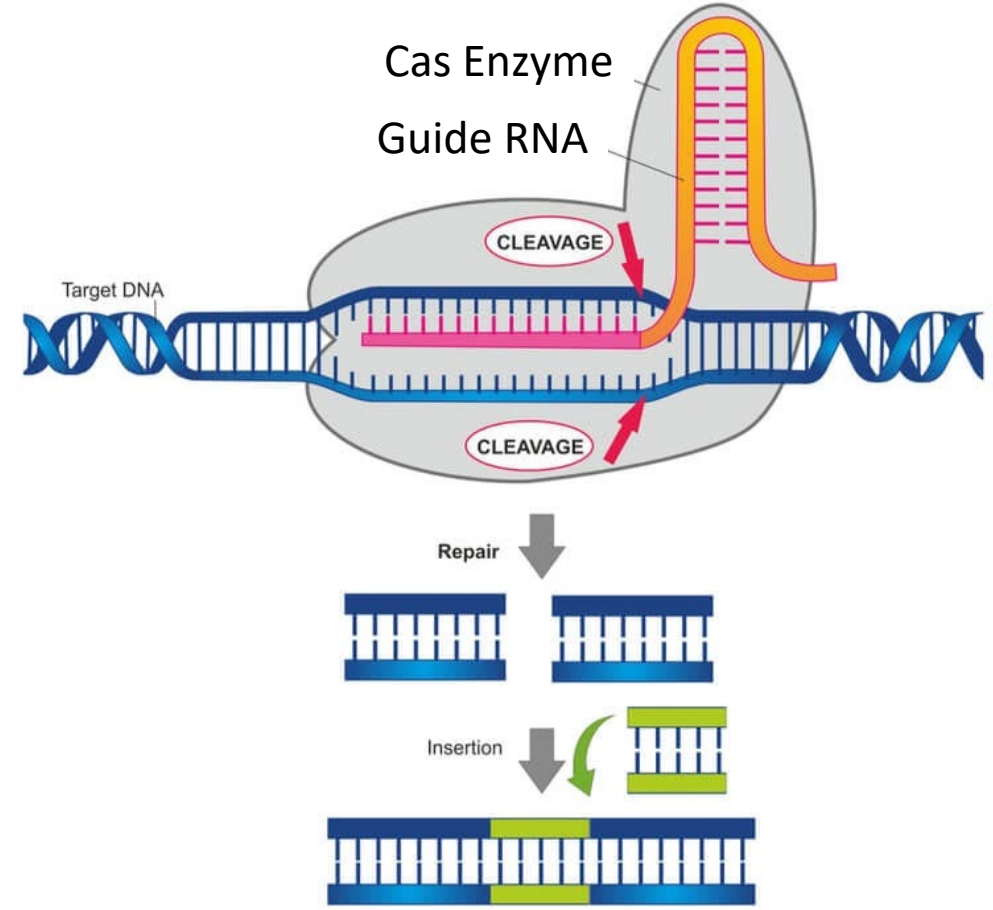
Timeline of CRISPR



Source: Hussen, B.M. *et al. Strategies to overcome the main challenges of the use of CRISPR/Cas9 as a replacement for cancer therapy*, 21 MOL. CANCER 64 (2022).

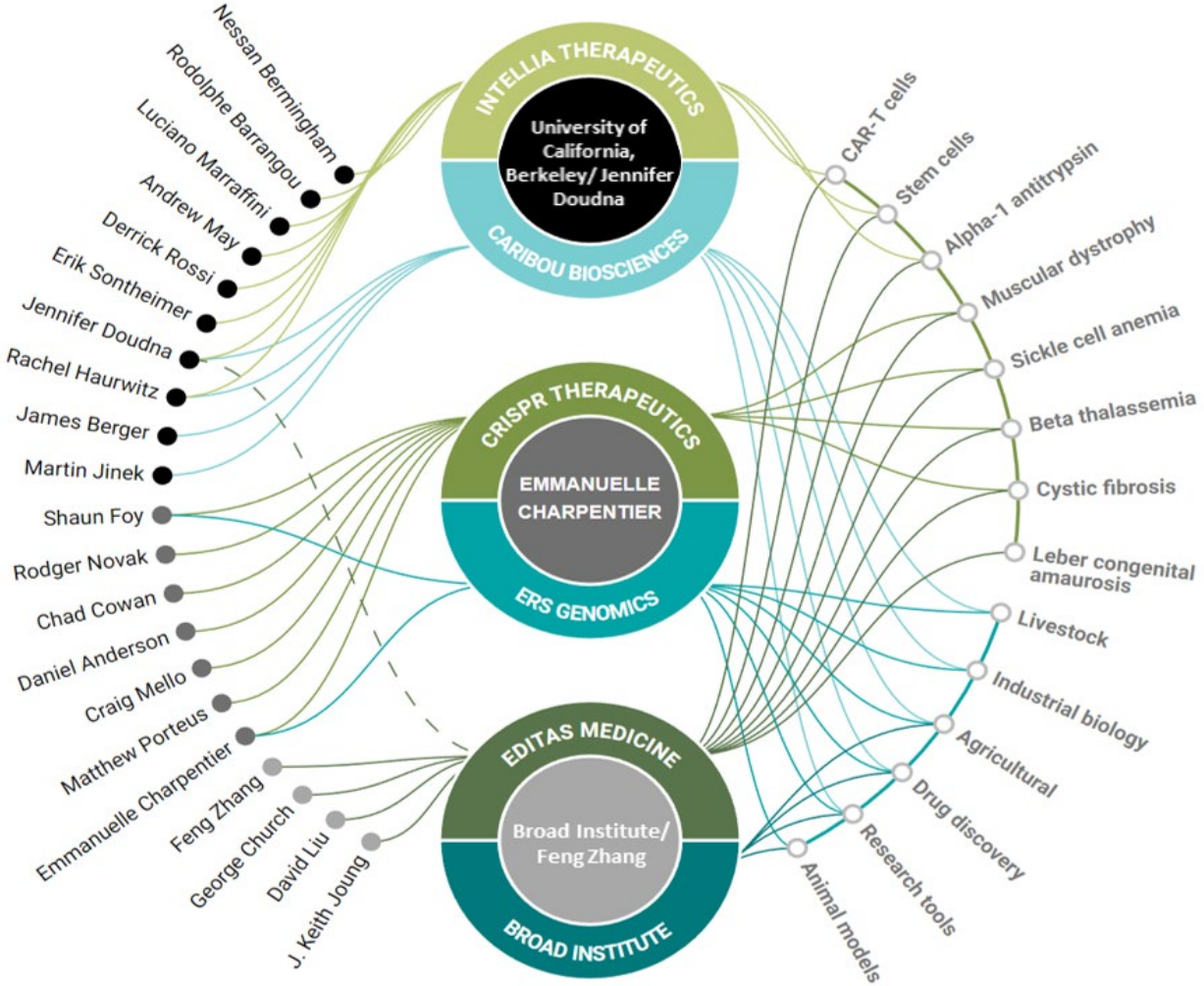
What is CRISPR?

"CRISPR": Clustered Regularly Interspaced Short Palindromic Repeats.

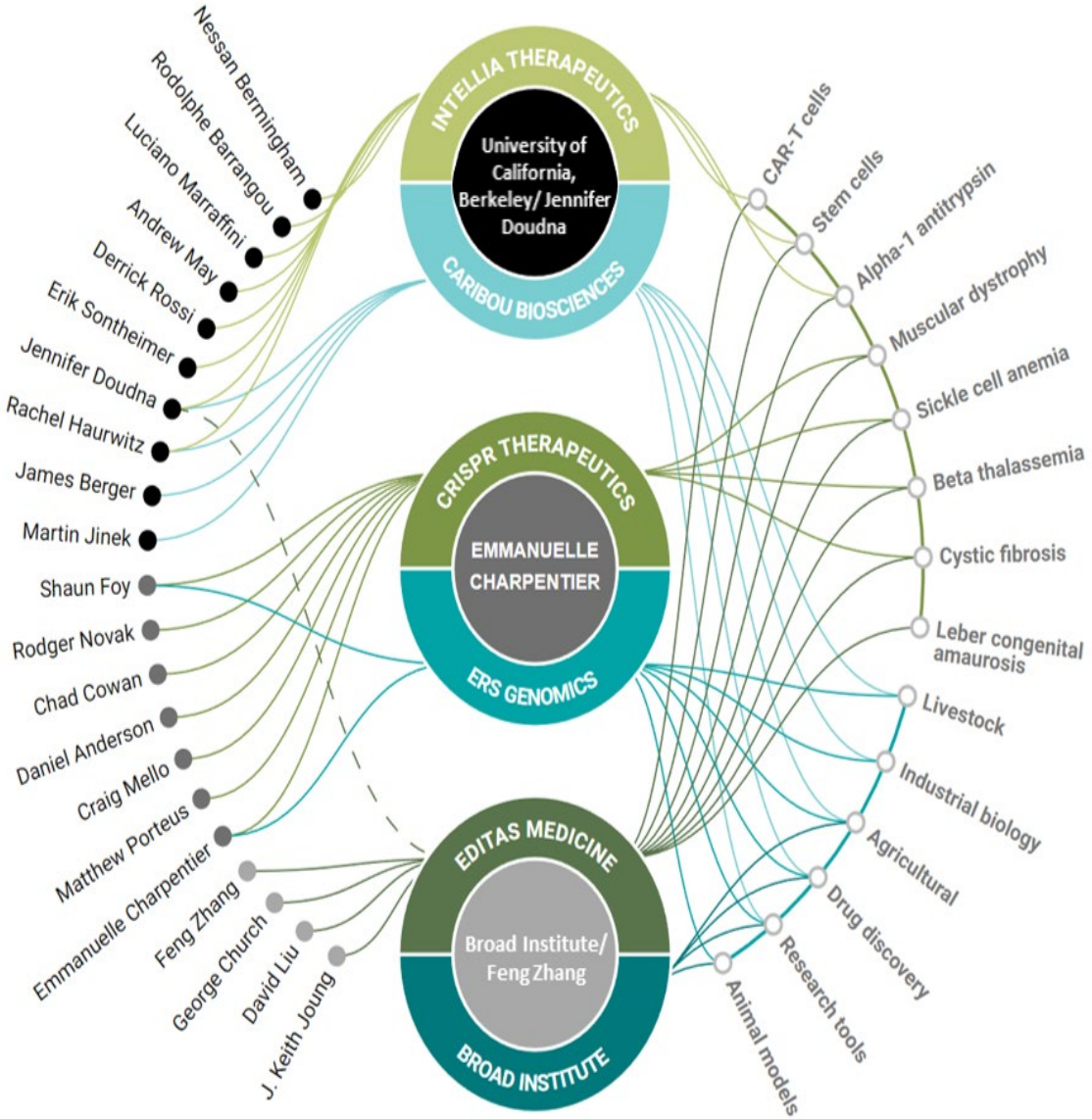


Source: Clara Rodríguez Fernández, *CRISPR-Cas9: The Gene Editing Tool Changing the World*; Labiotech (May 5, 2023).

Companies Specializing in CRISPR Therapies



Source: Jon Cohen, How the battle lines over CRISPR were drawn, Sci. (Feb. 15, 2017), https://www.science.org/content/article/how-battle-lines-over-crispr-were-drawn.



- Intellia Therapeutics
  - Market Cap = $3.84B
  - Number of Employees = 498
  - Total Assets = $1.52B (Annual)
- Caribou Biosciences
  - Market Cap = $274.91M
  - Number of Employees = 137
  - Total Assets = $373.77M (Annual)
- CRISPR Therapeutics
  - Market Cap = $4.77B
  - Number of Employees = 458
  - Total Assets = $2.24B (Annual)
- ERS Genomics
  - Private
- Editas Medicine
  - Market Cap = $608.54M
  - Number of Employees = 208
- Broad Institute
  - Non-profit

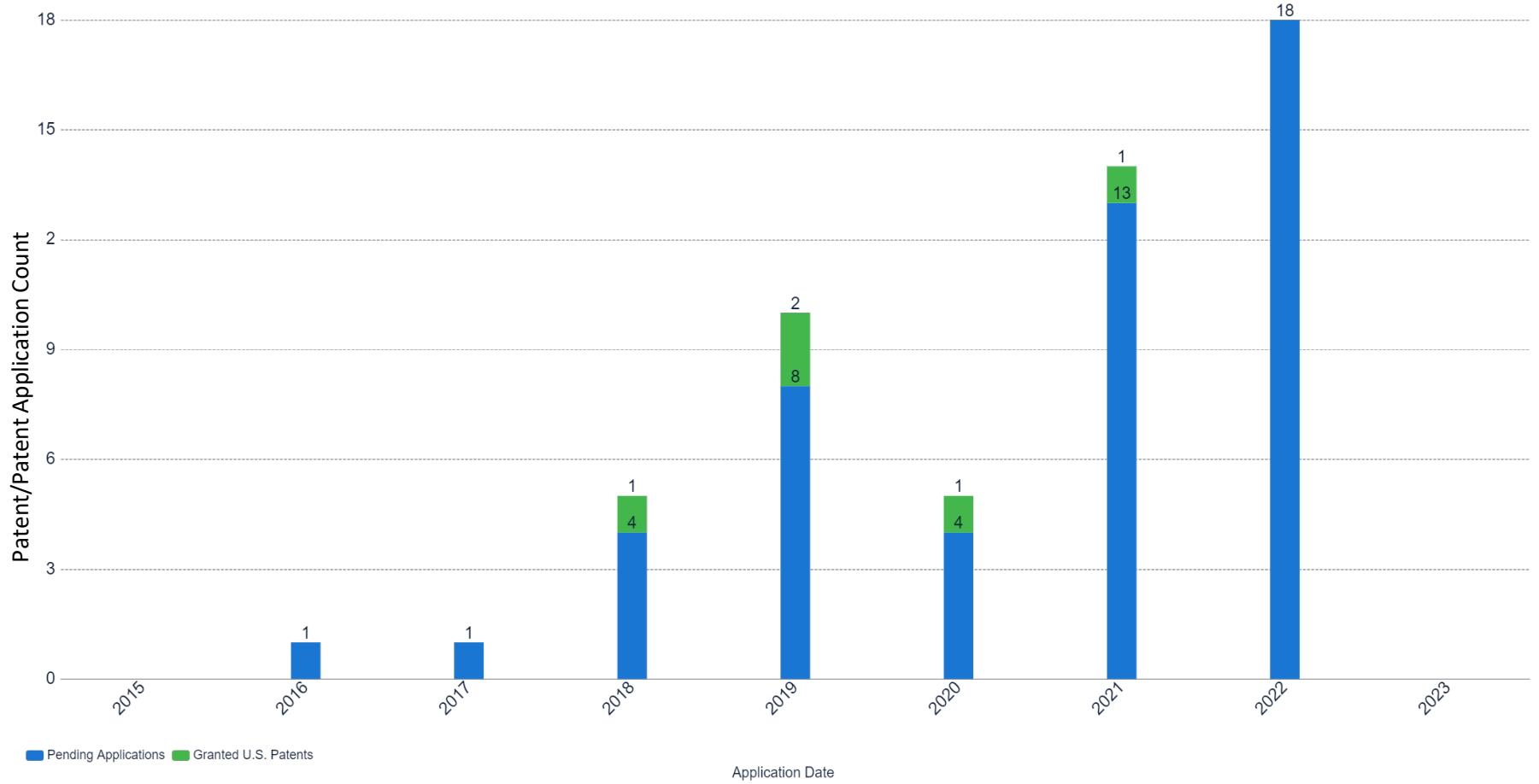
Source: Google Finance

CRISPR Therapy Updates in 2023

Company	Treatment	Indication	Event
CRISPR Therapeutics/Vertex Pharmaceuticals	Exa-cel	Sickle cell disease/Transfusion dependent beta thalassemia	BLA submission package complete by end of Q1 2023
Editas Medicine	EDIT-301	Sickle cell disease	Update for EDIT-301 Phase I/II trial by mid-2023
Graphite Bio	Nula-cel	Sickle cell disease	Proof-of-concept data for nula-cel by mid-2023
Intellia Therapeutics	NTLA-2002	Hereditary angioedema	Start of Phase II NTLA-2002 trial in H1 2023
Intellia Therapeutics	NTLA-3001	Alpha-1 antitrypsin deficiency	IND submission for NTLA-3001 in 2023
CRISPR Therapeutics	CTX310	Cardiovascular disease	CTX310 to move into clinical trial in 2023

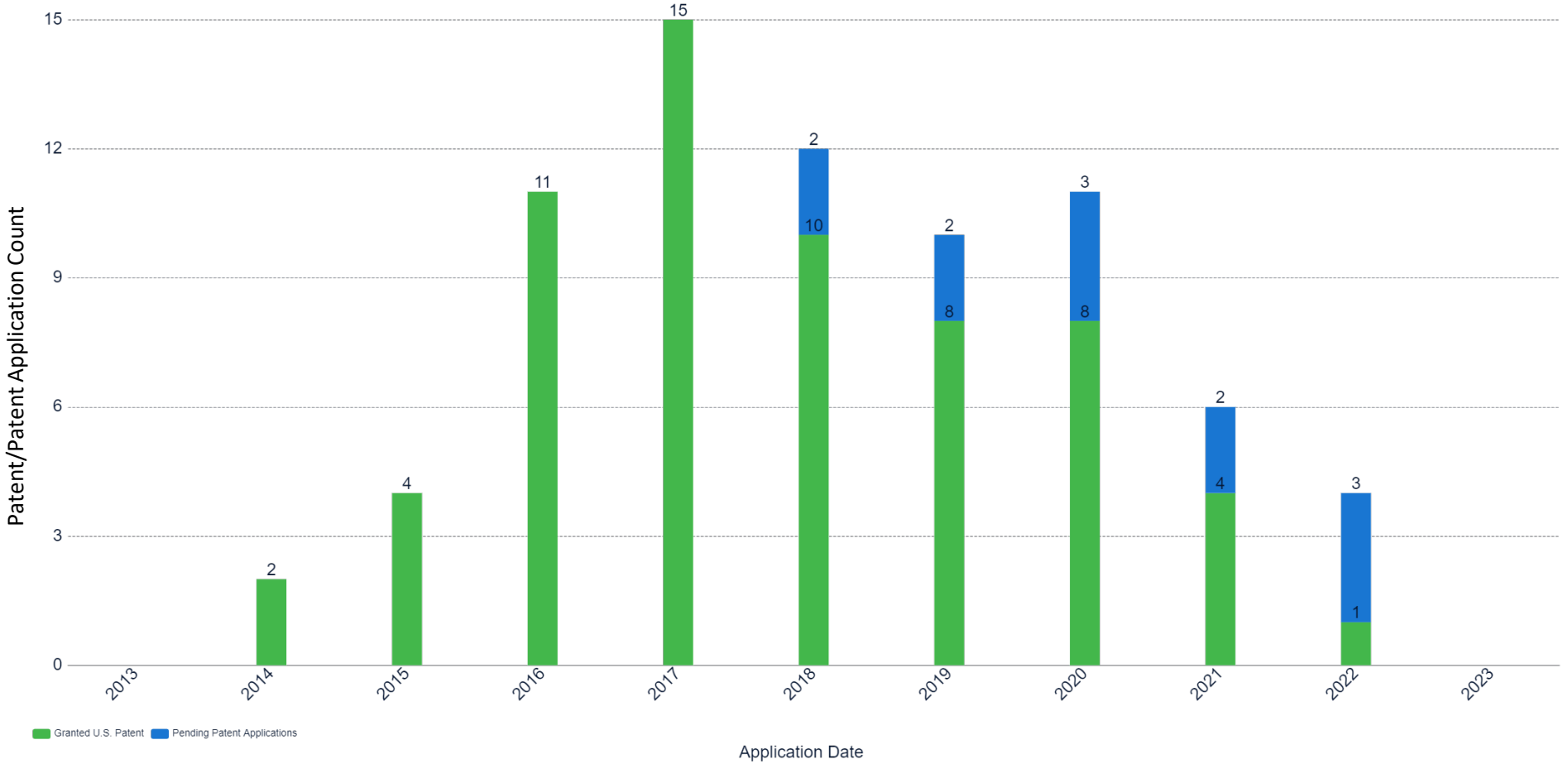
Source: GlobalData's Clinical Trials Database

Patent Portfolio



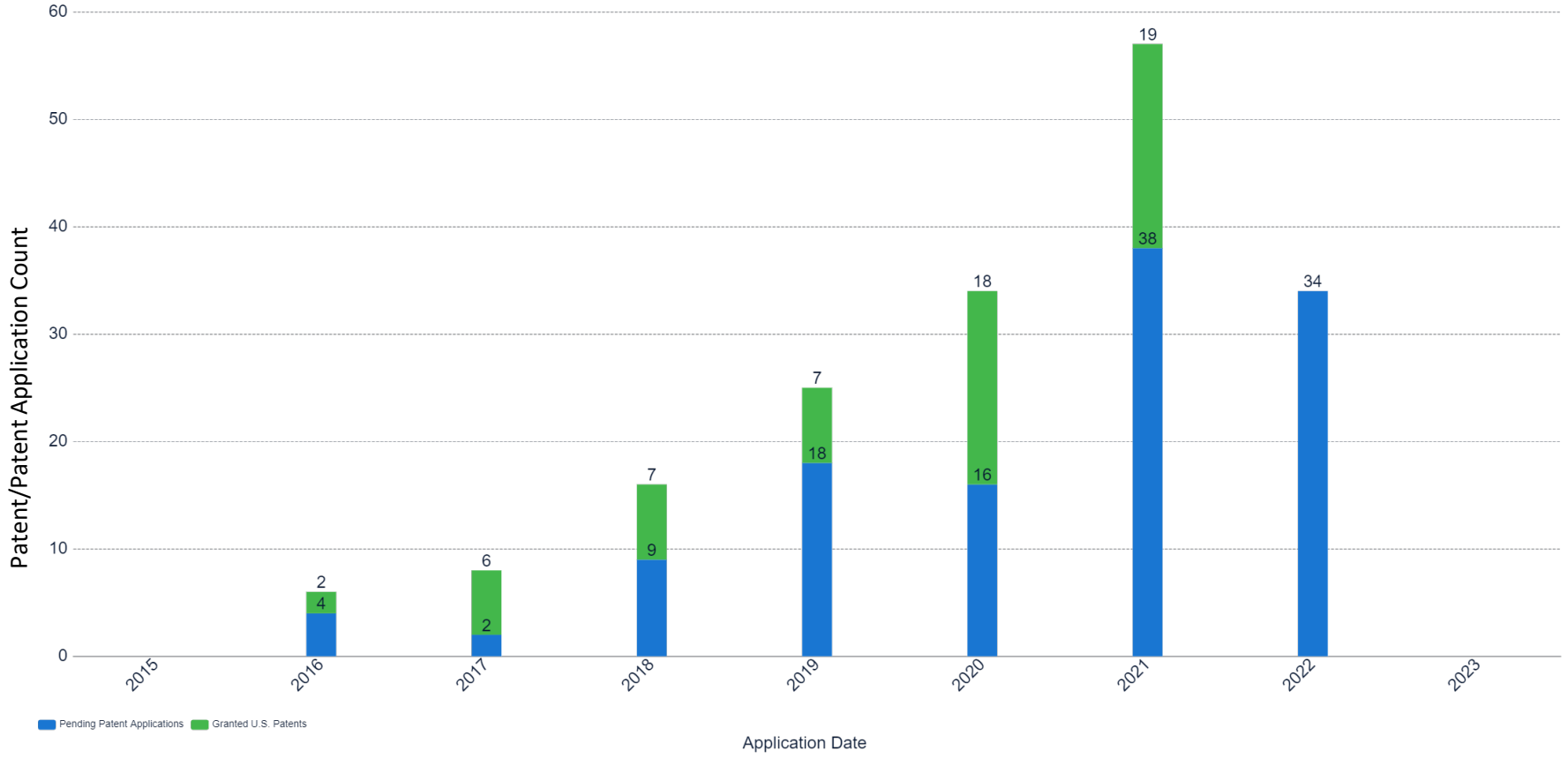
Source: Insights, Patsnap, June. 2023 (patent and patent application results generated using the keyword query: ALL_AN:("intellia")) within the U.S. and WIPO excluding inactive patents).

Patent Portfolio



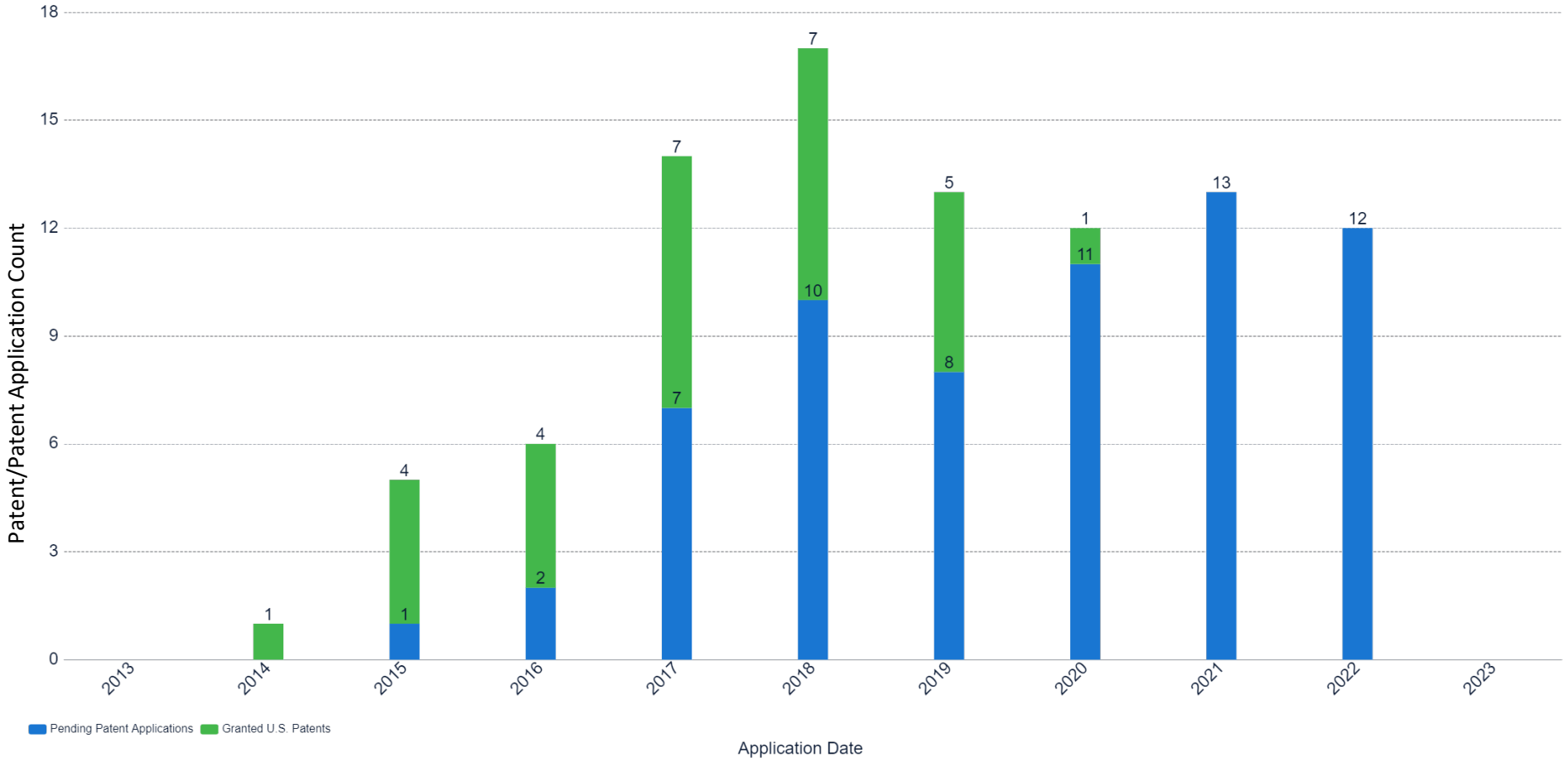
Source: Insights, Patsnap, Jun. 2023 (patent and patent application results generated using the keyword query: ALL_AN:("Caribou Biosciences") within the U.S. and WIPO excluding inactive patents).

Patent Portfolio



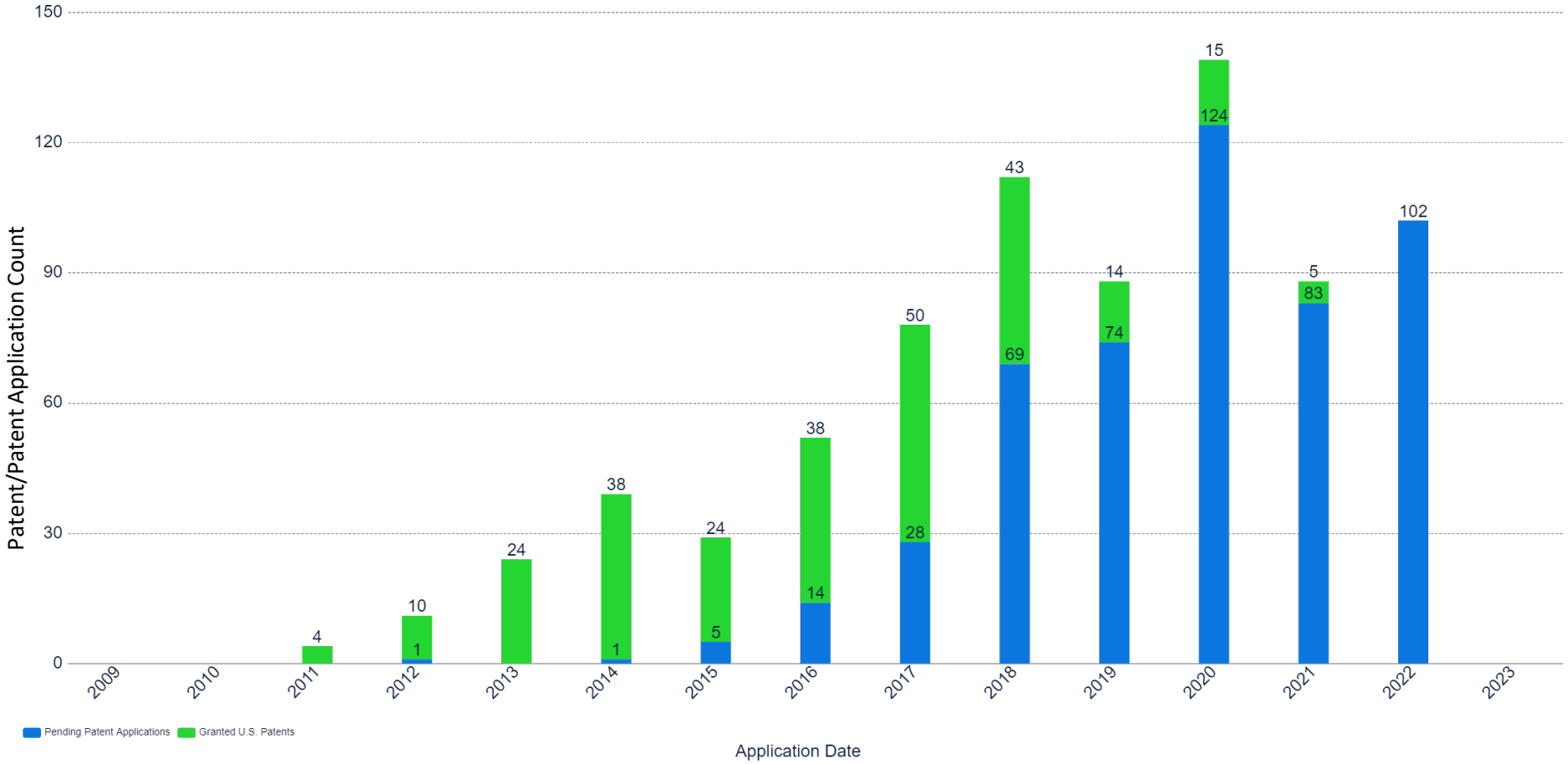
Source: Insights, Patsnap, June. 2023 (patent and patent application results generated using the keyword query: ALL_AN:("CRISPR Therapeutics") within the U.S. and WIPO excluding inactive patents).

Patent Portfolio



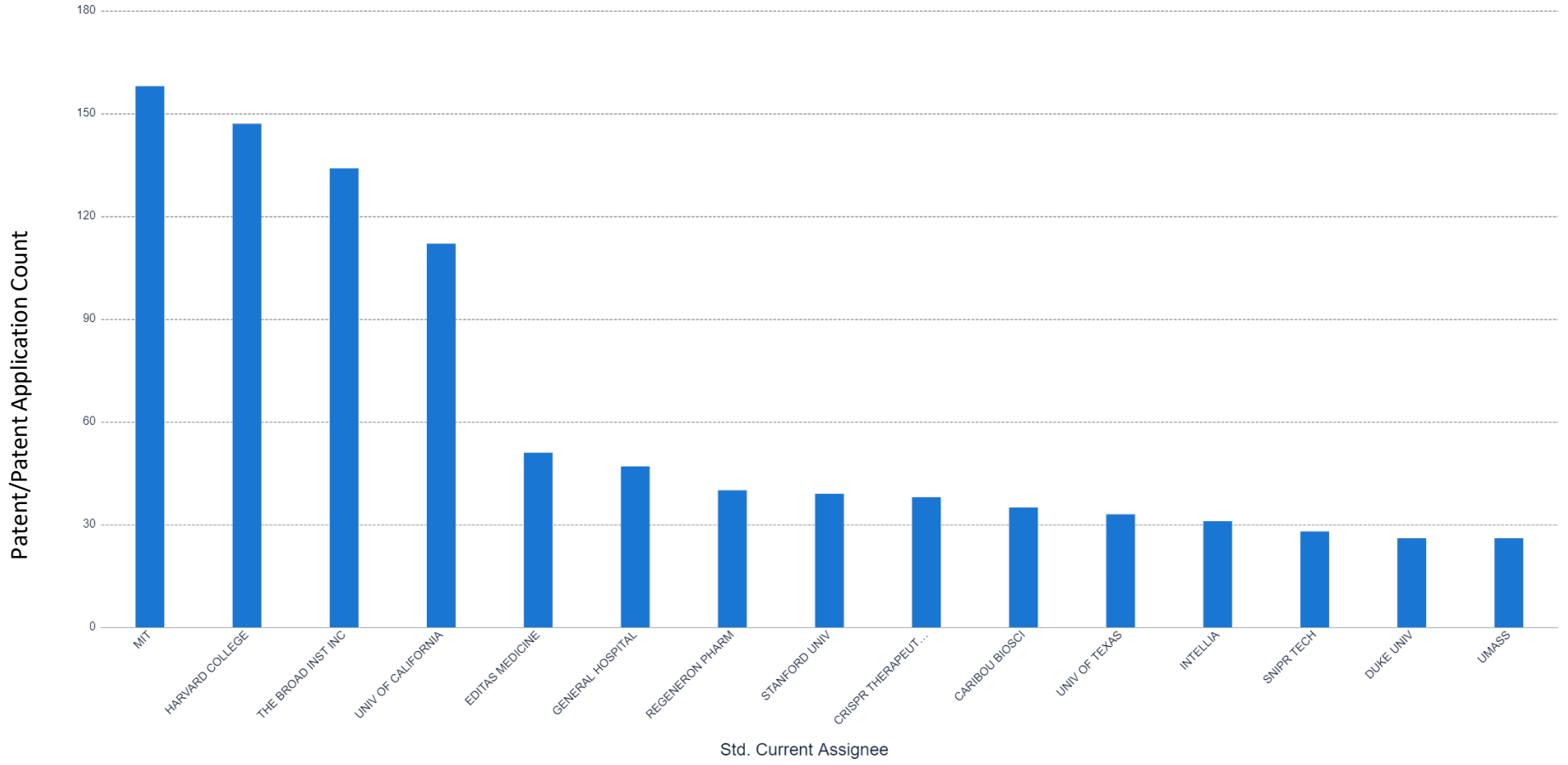
Source: Insights, Patsnap, June. 2023 (patent and patent application results generated using the keyword query: ALL_AN:(“Editas Medicine") within the U.S. and WIPO excluding inactive patents).

BROAD INSTITUTE Patent Portfolio



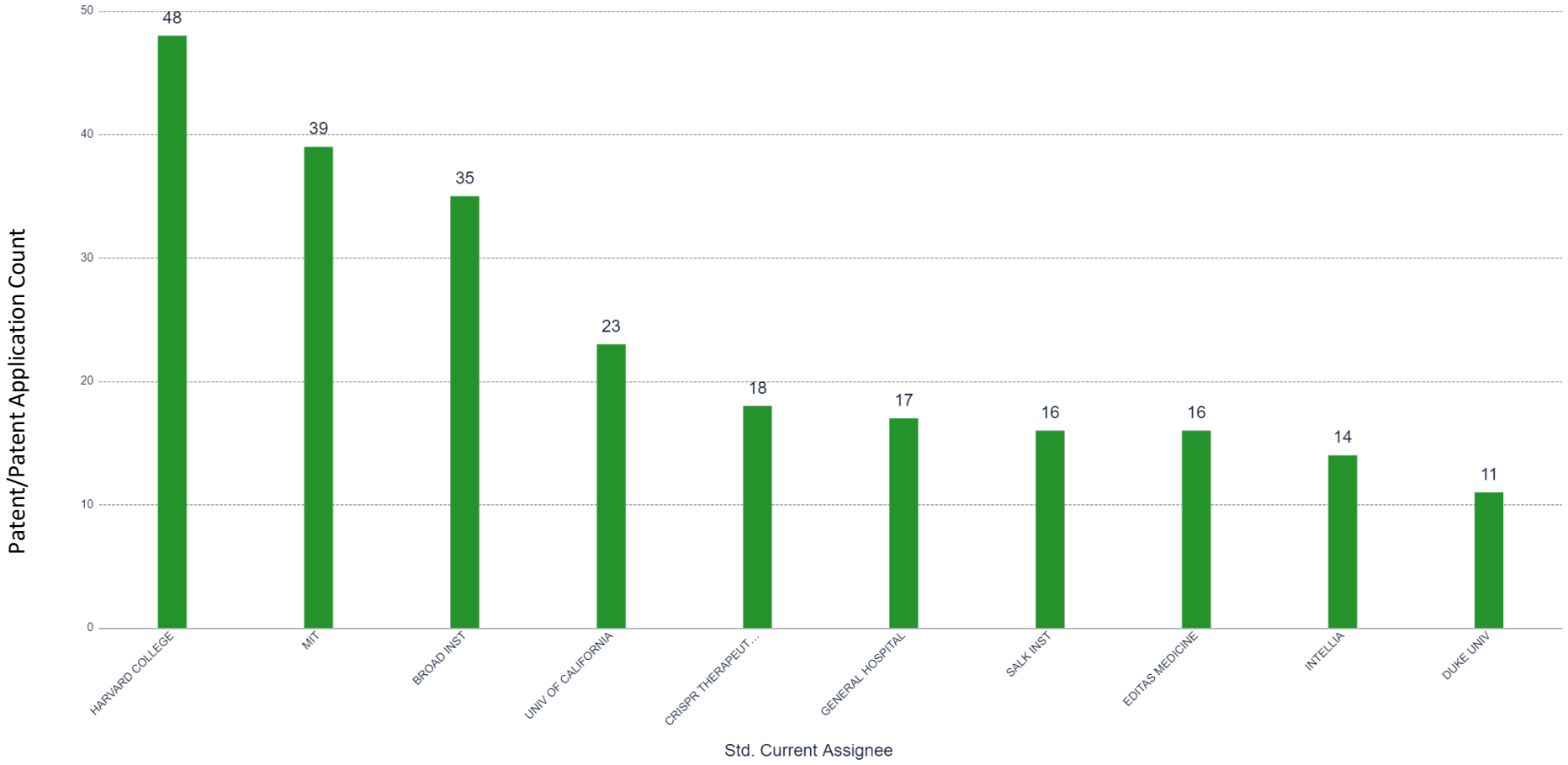
Source: Insights, Patsnap, June. 2023 (patent and patent application results generated using the keyword query: ALL_AN:("Broad Institute") within the U.S. and WIPO excluding inactive patents).

15 Largest CRISPR Patent Portfolios



Source: Insights, Patsnap, Jun. 2023 (patent and patent application results generated using the keyword query: TAC:("CRISPR" OR "Gene Editing" OR "guide RNA" OR "Cas*") AND IPC:(C12N2310/20 OR C12N15/07 OR C12N15/09 OR C12N15/113 OR C12N15/907 OR C12N15/63 OR C12N15/902) within the U.S. and WIPO excluding inactive patents).

Largest Guide RNA Patent Portfolios



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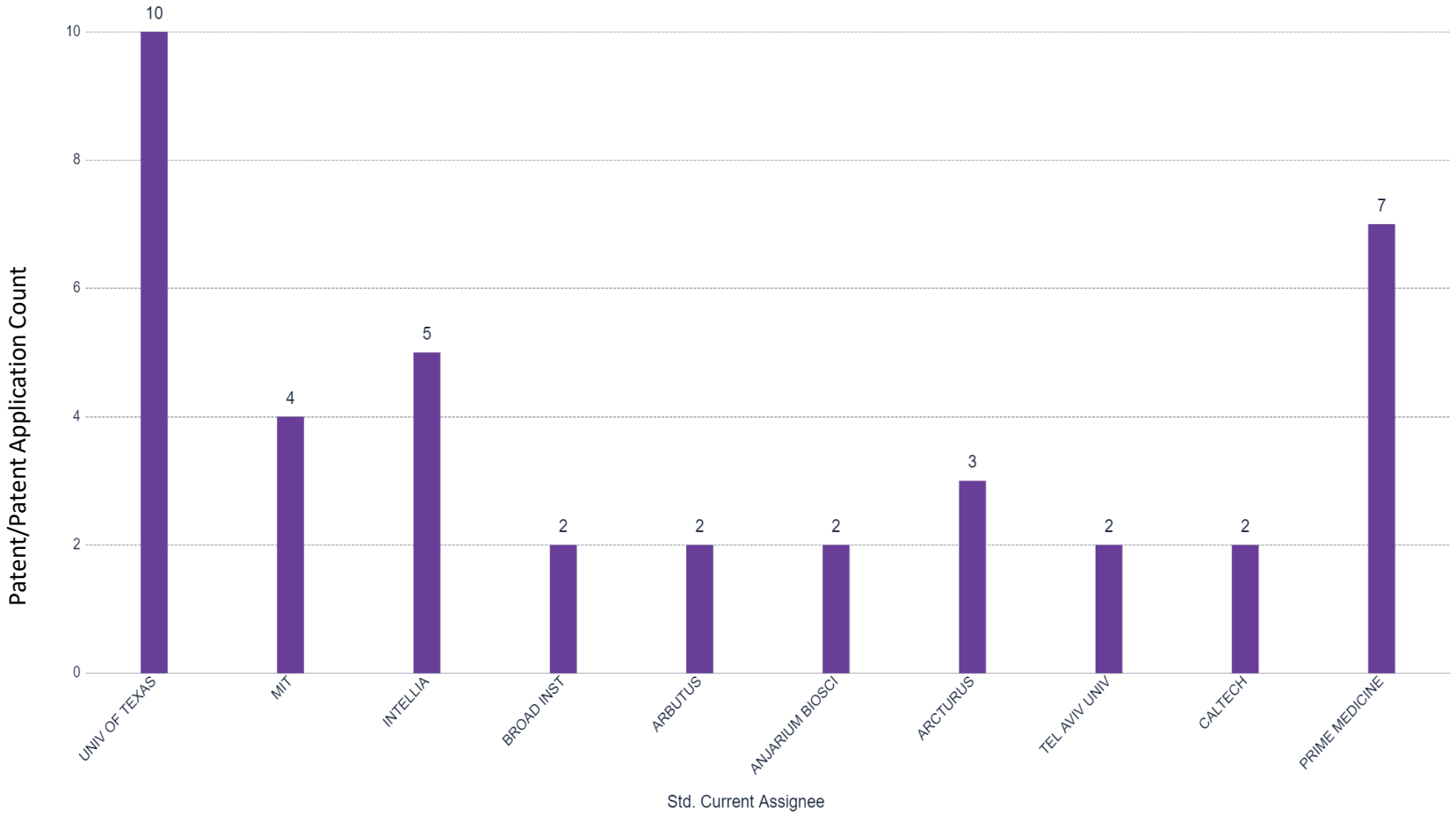
Largest LNP Patent Portfolios



Source: Insights, Patsnap, Jun. 2023 (patent and patent application results generated using the keyword query: TAC:("CRISPR" OR "Gene Editing" OR "Cas*" OR "guide RNA") AND ICLMS:("lipid*" OR "LNP") AND IPC:(C12N2310/20 OR C12N15/07 OR C12N15/09 OR C12N15/113 OR C12N15/907 OR C12N15/63 OR C12N15/902) within the U.S. and WIPO excluding inactive patents).

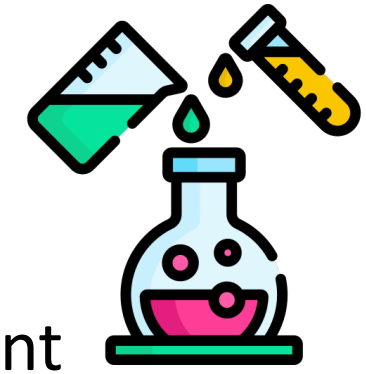
Top Challenges in the CRISPR Field

1. Crowded field.
   - There are more than 13,000 pending patent applications and patents globally on CRISPR-related technologies.
   - Anticipation and obviousness issues increase as the field gets more crowded, as do potential double patenting issues for mature portfolios.
2. Safety issues.
   - The FDA has put a study for a *in vivo* CRISPR-based gene editing on hold.[1]
   - Risk of off-target activity may cause genomic instability and disrupt the functionality of otherwise normal genes. [2]
3. Costs for developing gene therapy medicines are high:
   - Stocks of publicly traded biotechs soared to all-time highs during the COVID pandemic, but tumbled in 2021. Partially due to clinical and regulatory setbacks and rising funding costs. [3]

Top Five Considerations For a Successful Patent Application

1. What is the state of the art?
   - Is there already a similar product on the market, patent (or pending application), or published article describing a similar product?
   - What are the differences between your invention and the prior art?
   - Would your invention be considered obvious by a person of ordinary skill in the field in light of prior art?

Top Five Considerations For a Successful Patent Application



2. Do you have enough experimental data to support what you want to claim?
   - An application filed early without data may be insufficient to provide adequate written description and enablement.
   - Are you claiming too broadly? Do you have sufficient disclosures and examples to fully describe and enable the full scope of the claims?
   - However, can't wait too long- First inventor to file (with a sufficient disclosure) wins the race to get a patent.

Top Five Considerations For a Successful Patent Application

3. How far along is your invention?
   - Patent exclusivity lasts 20 years from the filing date—time filings to maximize sales or licensing revenues during the patent's exclusivity period.
   - Consider seeking additional patent protection on various aspects as further advancements or improvements are realized to build comprehensive portfolio.
   - Avoid creating prior art against your future filings by disclosing ideas early before they are ready for patenting.

Top Five Considerations For a Successful Patent Application

4. What is your exit strategy?
   - Out-License?
   - Develop it and sell asset/company?
   - Joint venture with a partner?
   - Commercialize it yourself?

5. What are the key markets?
   - Plan global patent strategy while developing technology.
   - Determine the list of countries where you will need patent protection.
   - Determine best types of protection to seek in those particular countries.
   - Budget for the costs of filing and seeking protection and product approvals in those markets.

THANK YOU

aharston@RFEM.com

swang@RFEM.com

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