Analyzing Rare Disease Trial Design Over Time:

exploring alternative trial design

Presenter:
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Clarivate Analytics

Analyzing rare disease trial design over time

In this session the questions we will also address include:

- Can I analyze granular clinical trials information at the gene variant or patient segment level?
- How does my patient segmentation strategy affect trial success?
- What are the trial timelines for rare disease trials and how have they changed over time?
- Can I analyze rare diseases from a global perspective to find the sites that can enroll the patients I need?
- Where are the unmet needs in rare diseases and niche patient populations?
- How can I determine where my highest competition will be for site selection?

Source: Cortellis Clinical Trials Intelligence

Trial Overview	Competitive and timeline insights	Clinical Development	Clinical Operations
◦ Condition ◦ Interventions ◦ Phase ◦ Recruitment Status ◦ Action ◦ Class ◦ Category ◦ Design ◦ Pioneer Conditions ◦ Interventions Alone ◦ Interventions In Combination ◦ Active Control ◦ Registry Source ◦ Document Source ◦ Added Date ◦ Last Change Date	◦ Sponsors / Collaborators ◦ Organization Type ◦ Sponsor Only ◦ Collaborator Only ◦ Commercially Relevant ◦ Start Date ◦ End Date ◦ Primary Endpoint Completion Date	◦ Patient Segment ◦ Biomarker ◦ Biomarker Type ◦ Biomarker Role ◦ Age / Race / Healthy Volunteers ◦ Inclusion Criteria ◦ Exclusion Criteria ◦ Endpoint Types ◦ Endpoints ◦ Primary Endpoints ◦ Secondary Endpoints ◦ Results Available ◦ Endpoints Met ◦ Adverse Events	◦ Site Name ◦ Contact Name ◦ City ◦ State / Province / County ◦ Country ◦ Region ◦ Enrolment End Date ◦ Enrolment Count ◦ Enrolment Rate

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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Challenges in Rare Disease Trials

The International Rare Disease Research Consortium (IRDiRC) stated an objective to contribute to the development of 200 new rare disease treatments by 2020- This was achieved in 2017… 3 years early

- Rate of occurrence and poor natural disease history
- Small patient populations
- Hard to identify patients, especially early on in disease progression
- Many affect pediatric populations
- Widely dispersed geographically
- Already a large emotional and financial burden on rare disease patients and families
- Too far for patients to travel to nearest enrollment site
- Traditional trial designs are not effective
- International trial design leads to complex regulatory situations

As part of the new IRDiRC vision, 1000 new therapies are to be approved by 2027. The goal is for the majority to be for diseases with out currently approved therapies

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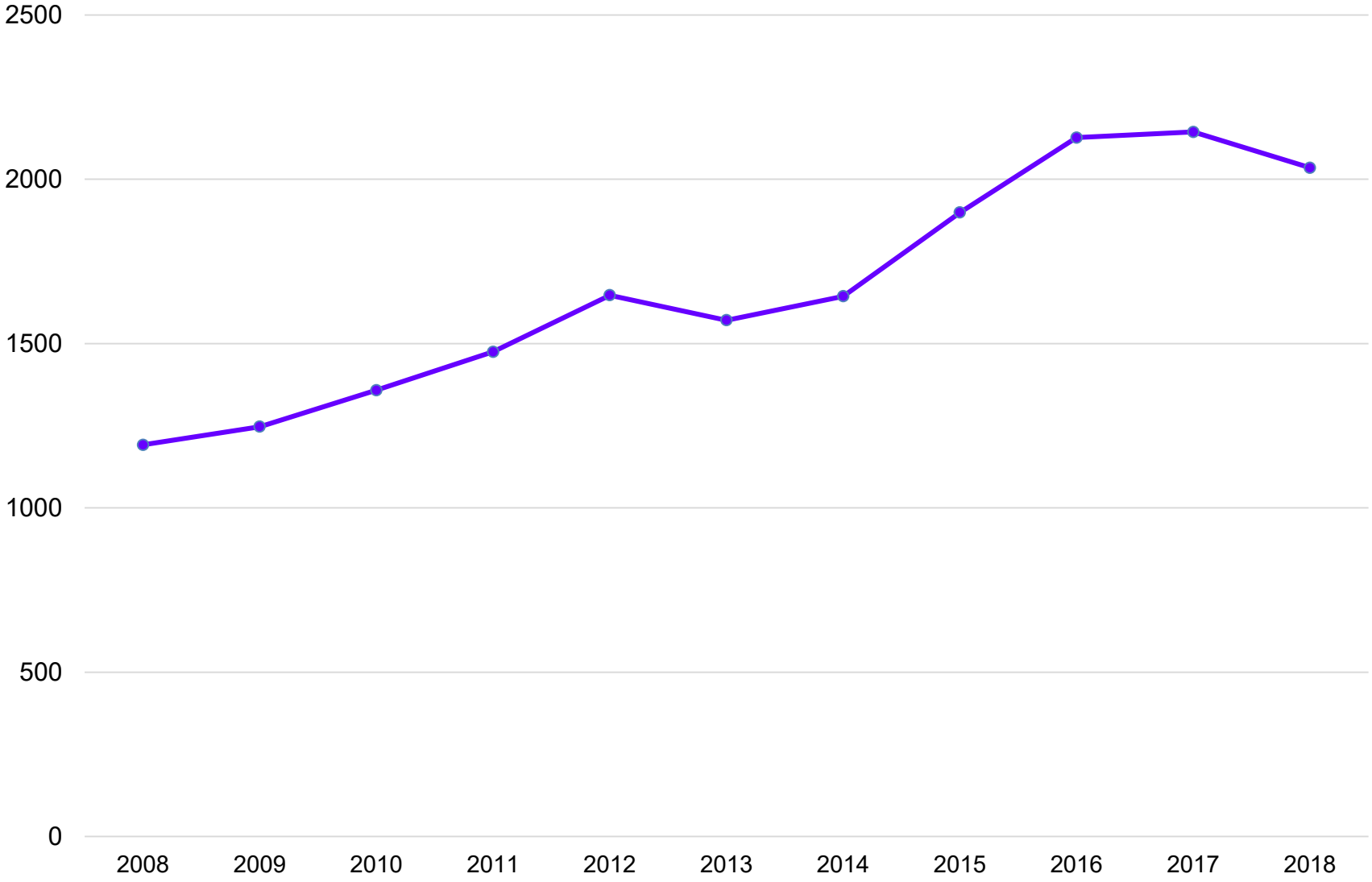
Source: http://www.irdirc.org

Rare Disease Trials



Data are shown for number of Rare Disease Trials each year, phase 1-4 with a start date of 2008 - 2018 and includes completed, ongoing, and terminated studies. Note that it does not show cumulative total trials.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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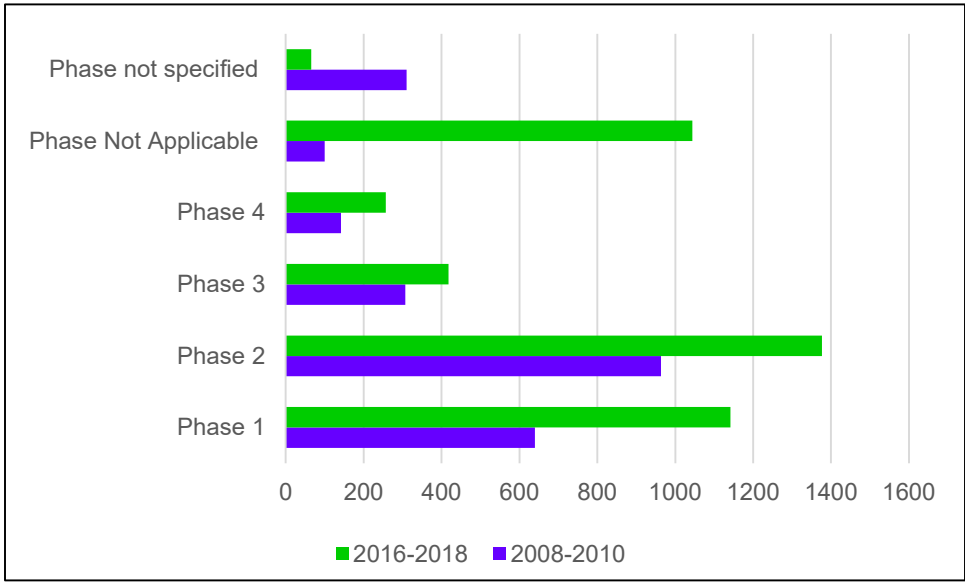
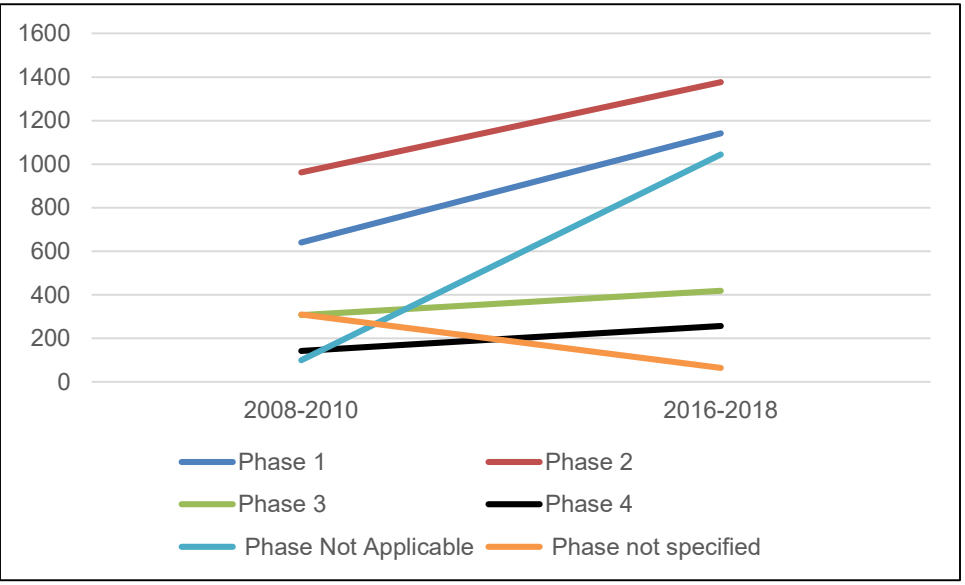
Rare Disease Trials by Phase

- According to the Centers for Medical Research (CMR) the probability of success moving from phase 1 to market is less than 10% across all Therapy Areas
- The need for rare disease trials to be accelerated in order to meet unmet patient need may have led to alternative trial design



2008-2010= # trials with start date 1/1/2008-1/1/2010
2016-2018= # trials with start date 7/1/2016-7/1/2018



- The number of trials that are classified as ‘phase not applicable’ has grown notably in the last 10 years

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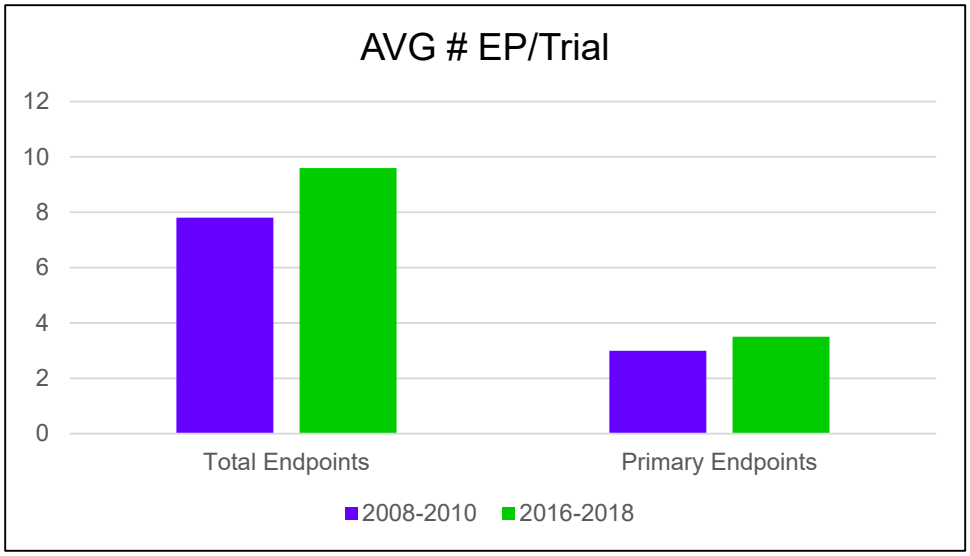
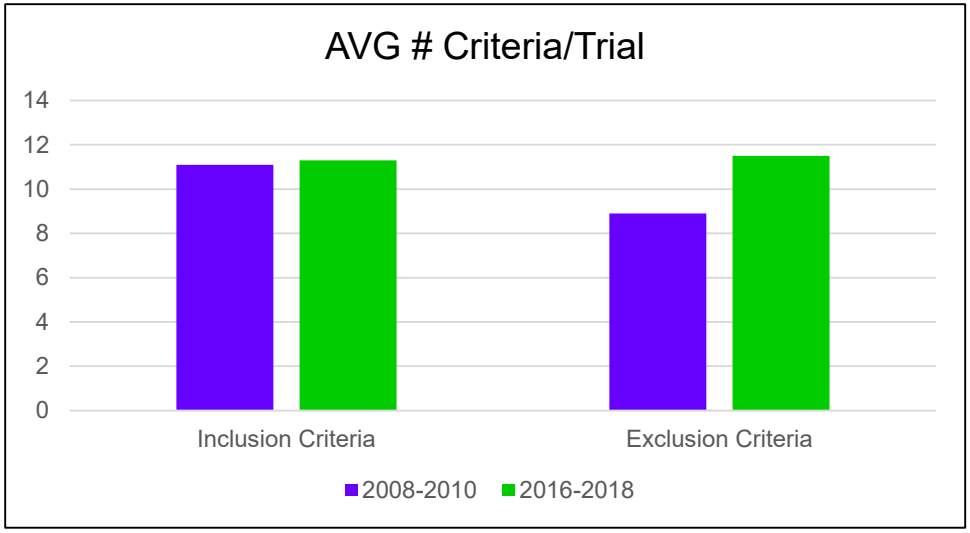
Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence, CMR

Design Trends: Has trial design been simplified as the need for larger enrollment numbers increases?





- An overall increase in average # of endpoints per trial has been seen in the past 10 years
- An increase in average # of exclusion criteria per trial has been seen in the past 10 years
- A slight increase in average # of inclusion criteria per trial has been observed, though it is less of an increase than other trial components. Could this be due to a stronger focus on patient segmentation?

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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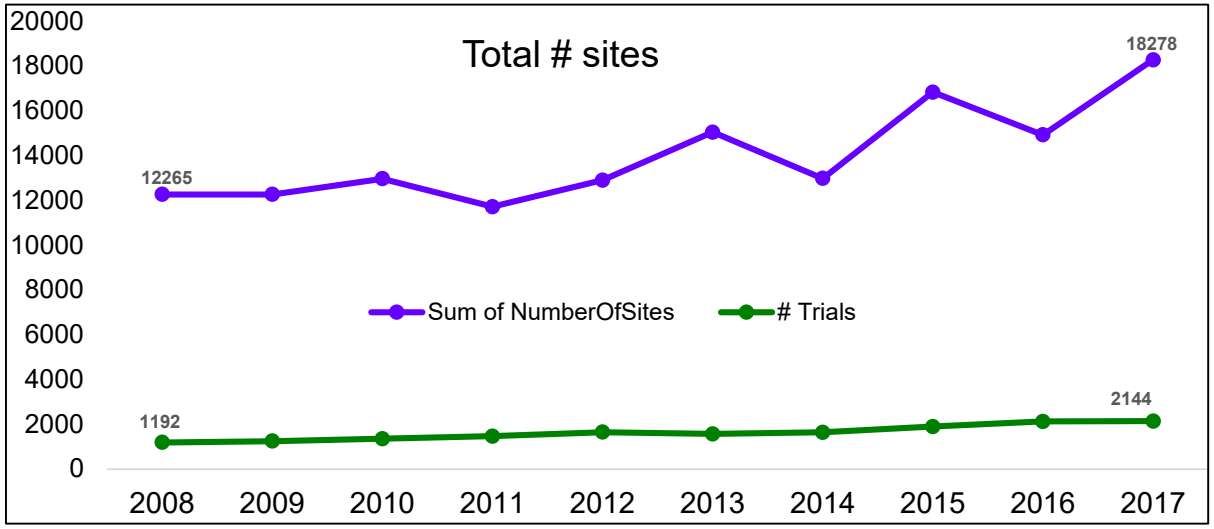
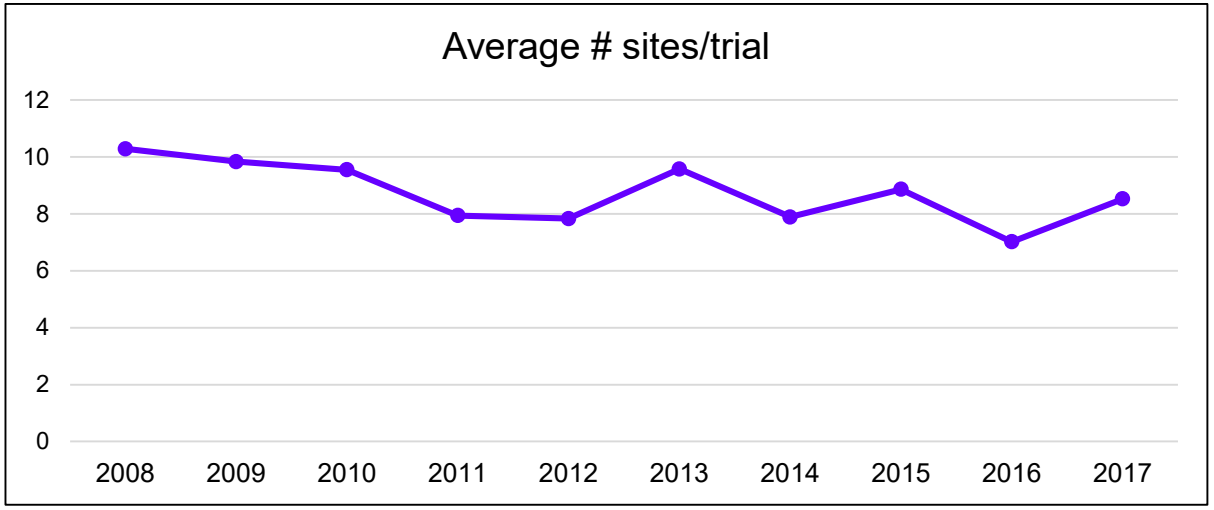
Site Data: Have the # of sites participating in rare disease trials increased to accommodate larger patient enrollment goals?





- Is there a need in the rare disease space to increase the number of sites available to decrease patient burden and increase patient participation?
- *Although in the past 10 years there are **more than 6,000** sites participating in current trials than there were 10 years ago, the overall trend shows that the **average # of sites per trial** has actually **decreased** over time*
- Are sponsors getting better at choosing high enrolling sites? Are they choosing sites more fitted for the right patient segments? Are the geographic location of those sites more strategically placed?
- Is there still a need to identify more sites to participate to ultimately reach more rare disease patients?

Site data is sourced from global trial registries for all completed, ongoing, and terminated/suspended trials per year. Number of trials per year = start date within the calendar year.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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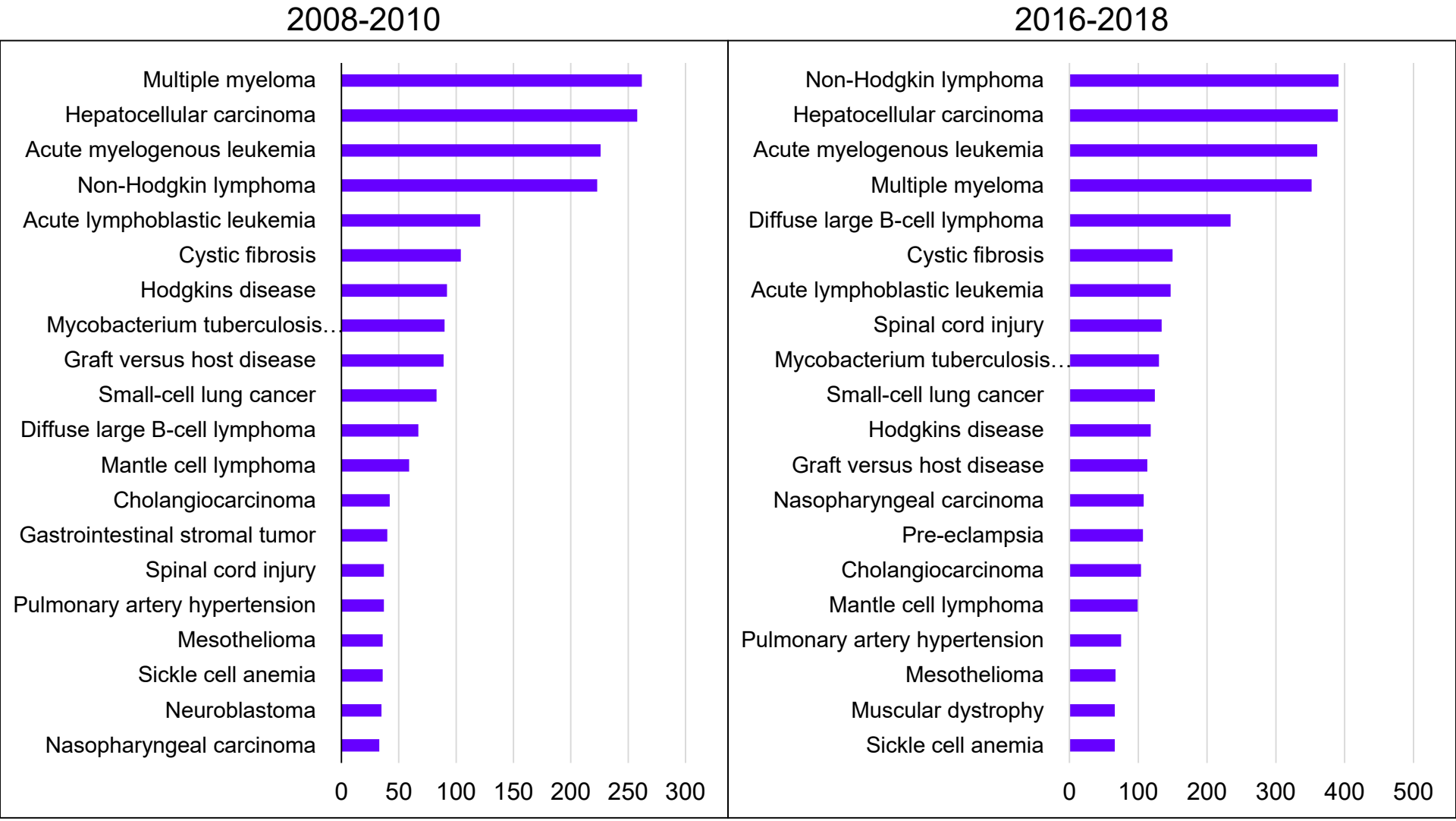
Top 20 Rare Diseases



Data shown represents trials per time period where the disease shown is one of the active conditions being studied in the trial.
Number of trials per time period per condition = start date within 1/1/2008- 1/1/2010 and 7/1/2016-7/1/2018.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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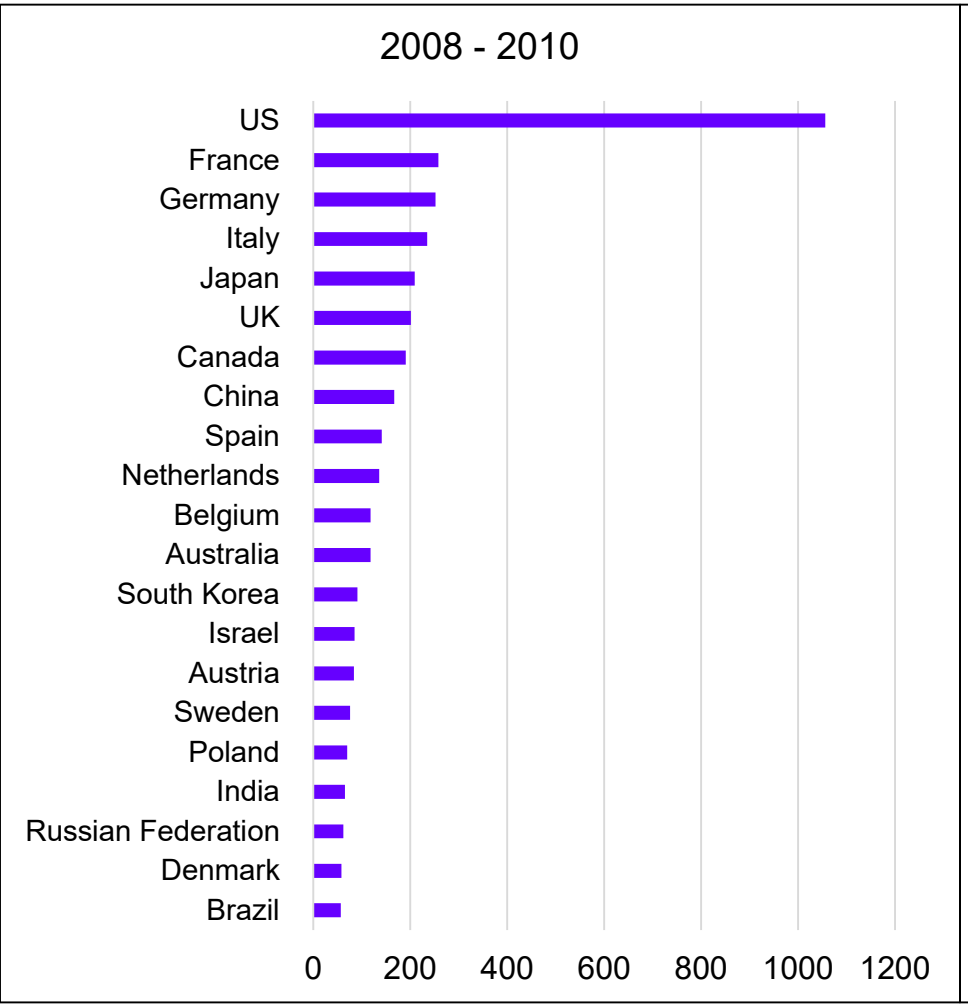
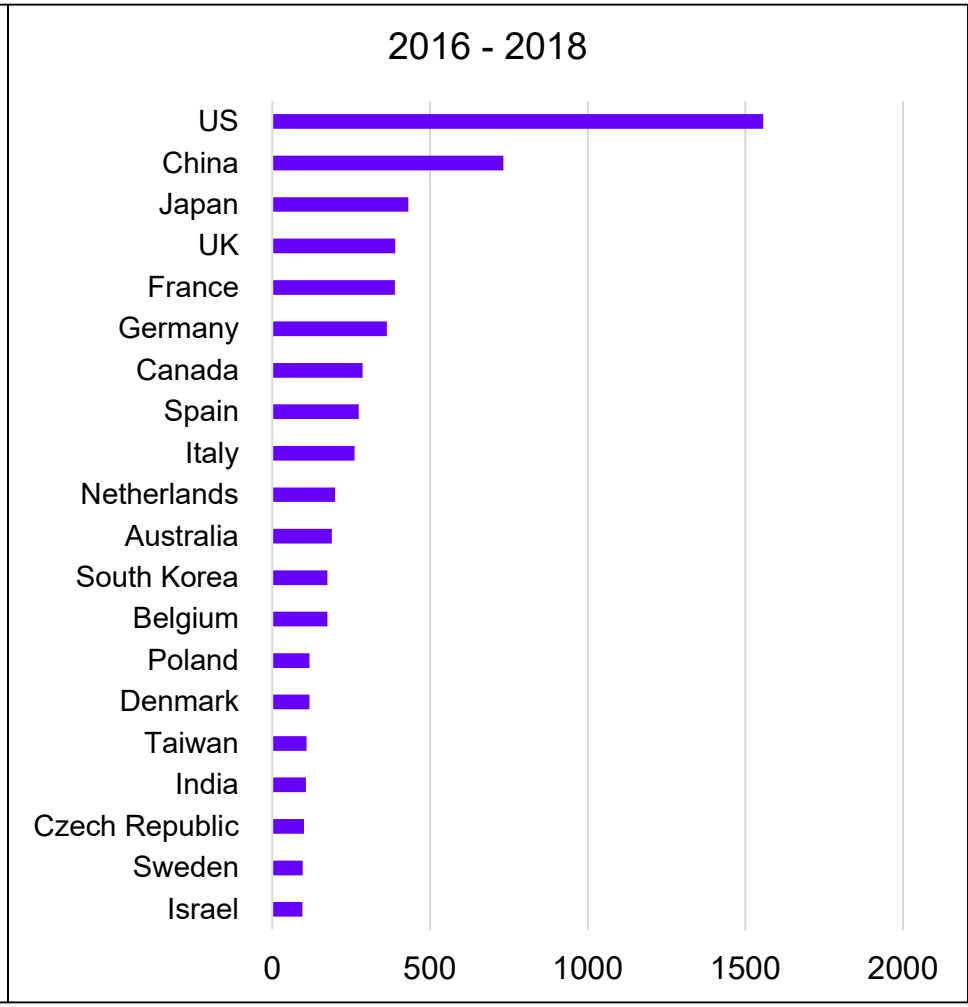
Locations by Country





Data shown represents locations of trials per time period. Number of trials per time period per location = start date within 1/1/2008-1/1/2010 and 7/1/2016-7/1/2018.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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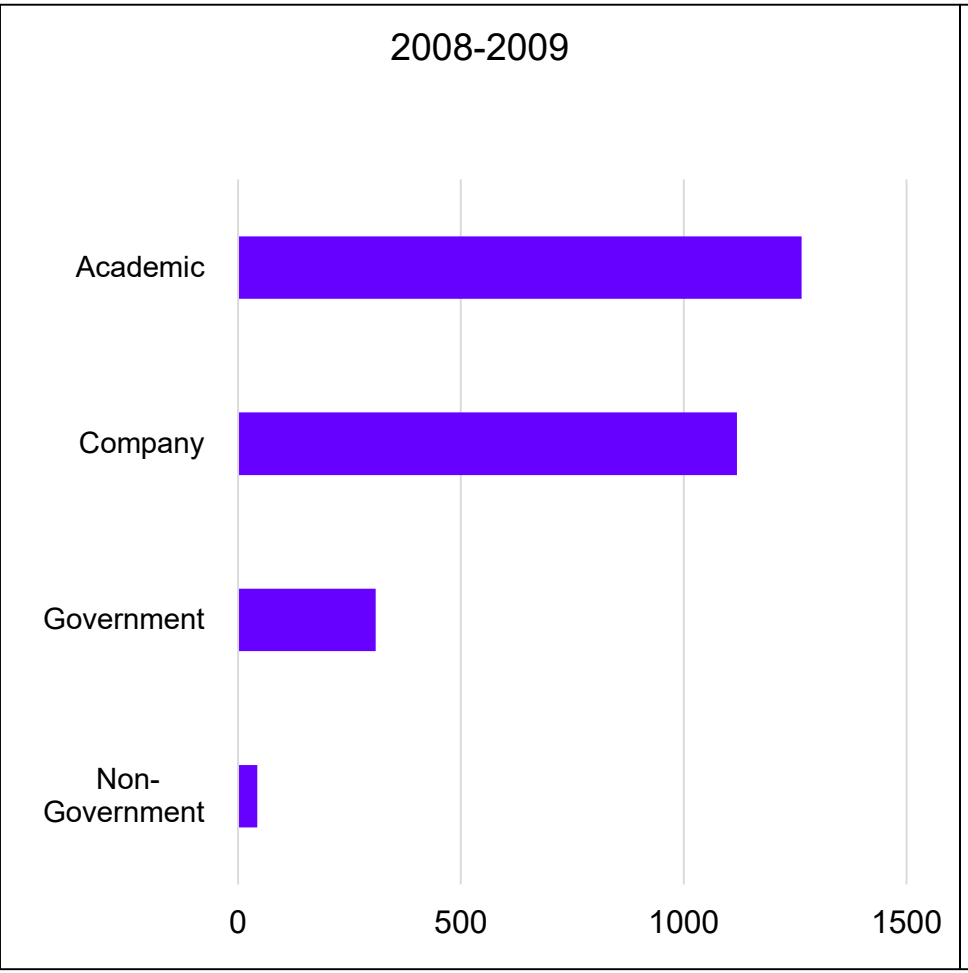
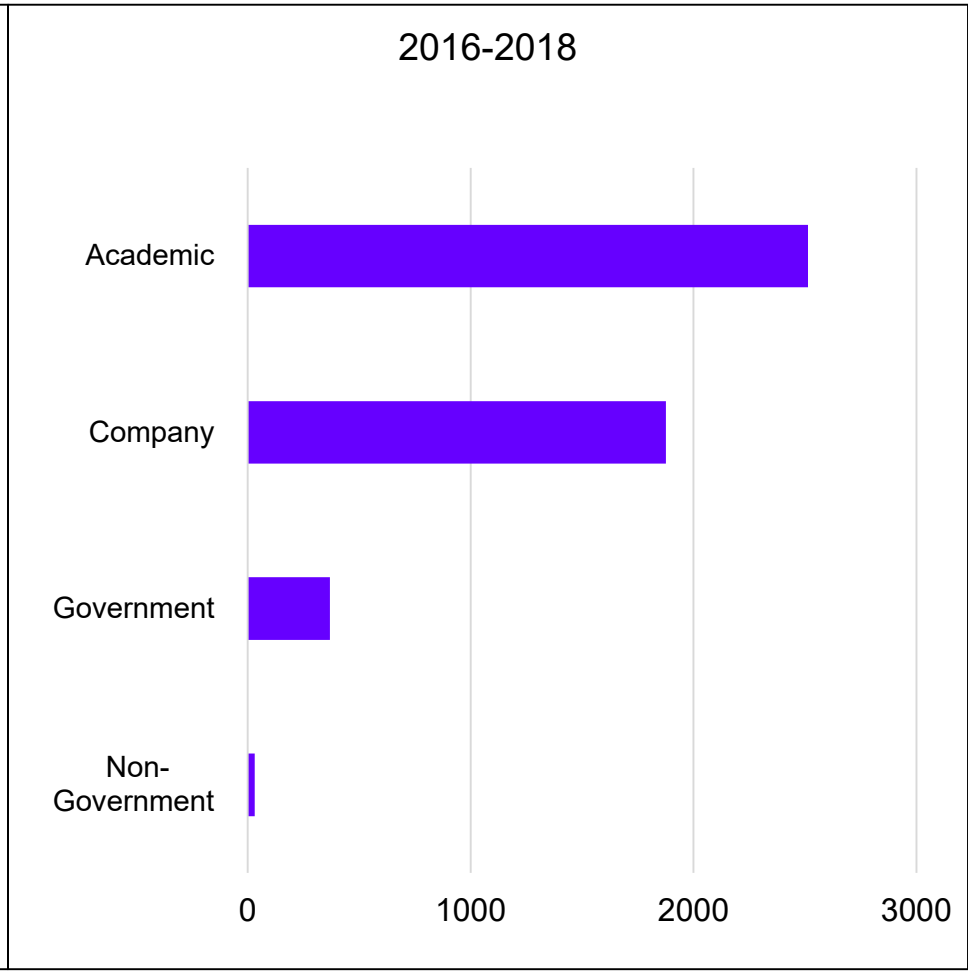
Sponsor Type





Data shown represents trials per time period per sponsor type. Number of trials per time period = start date within 1/1/2008-1/1/2010 and 7/1/2016-7/1/2018.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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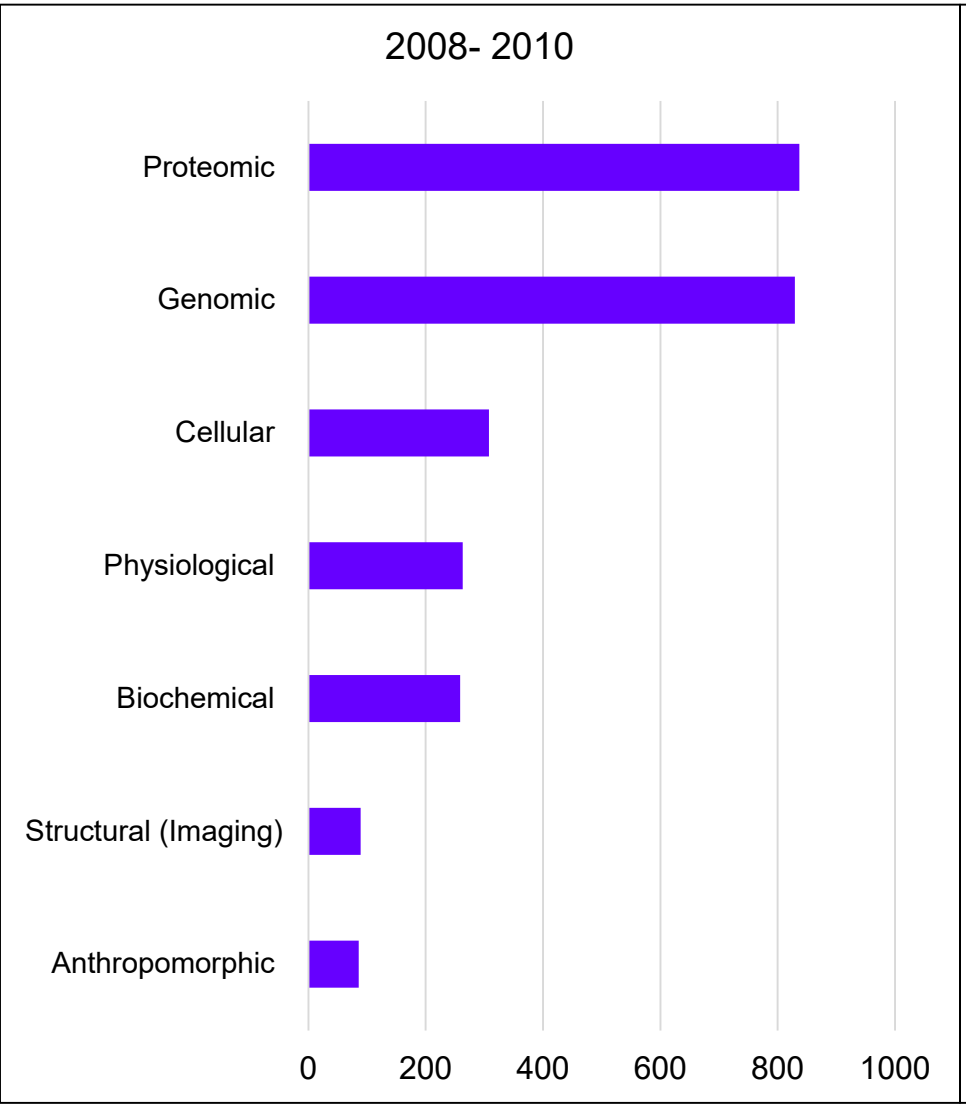
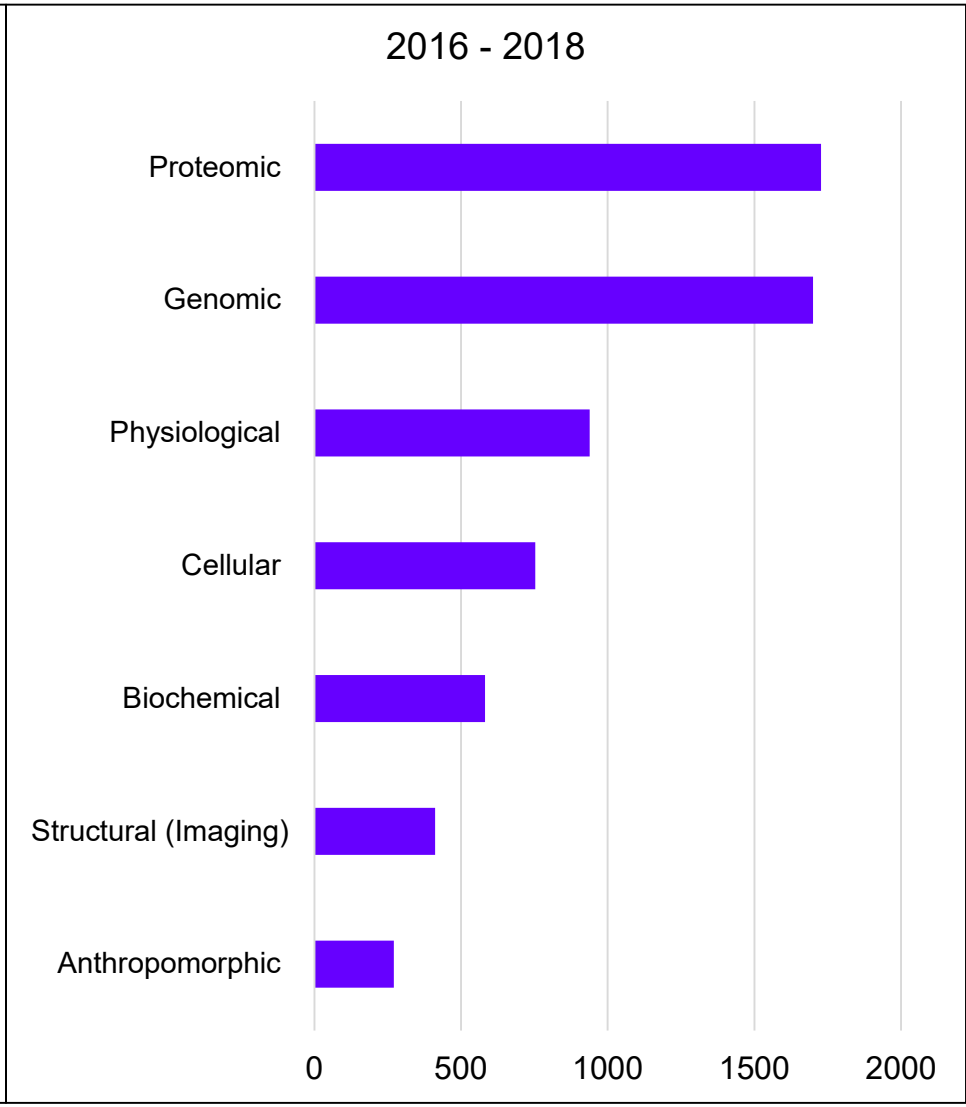
Biomarker Type





Data shown represents trials per time period where one of the biomarker types is being studied. Number of trials per time period = start date within 1/1/2008- 1/1/2010 and 7/1/2016-7/1/2018.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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Additional Analysis

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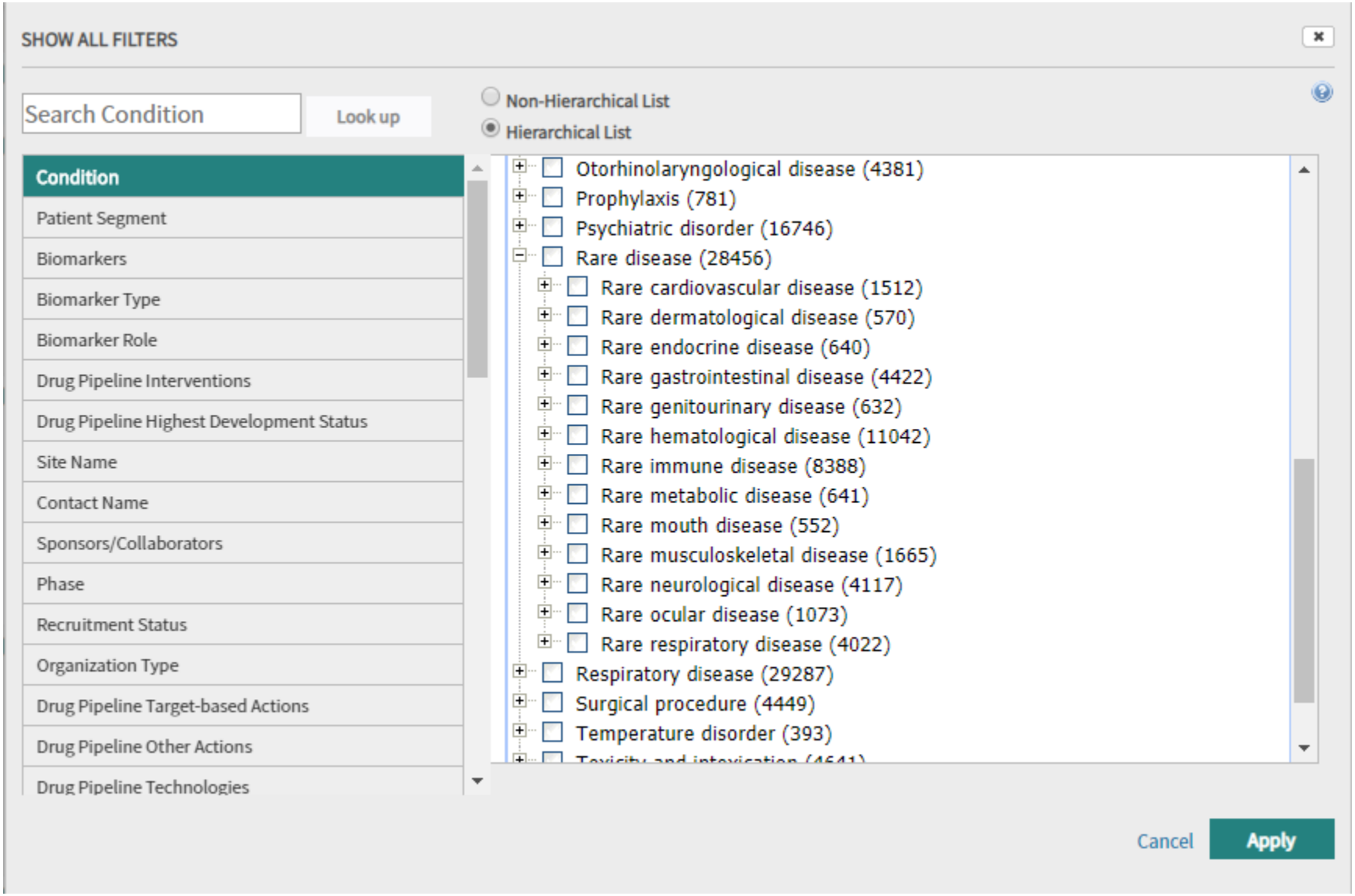

Cortellis Clinical Trials Intelligence covers over 28,000 rare disease trials mapped to 435 orphanet terms.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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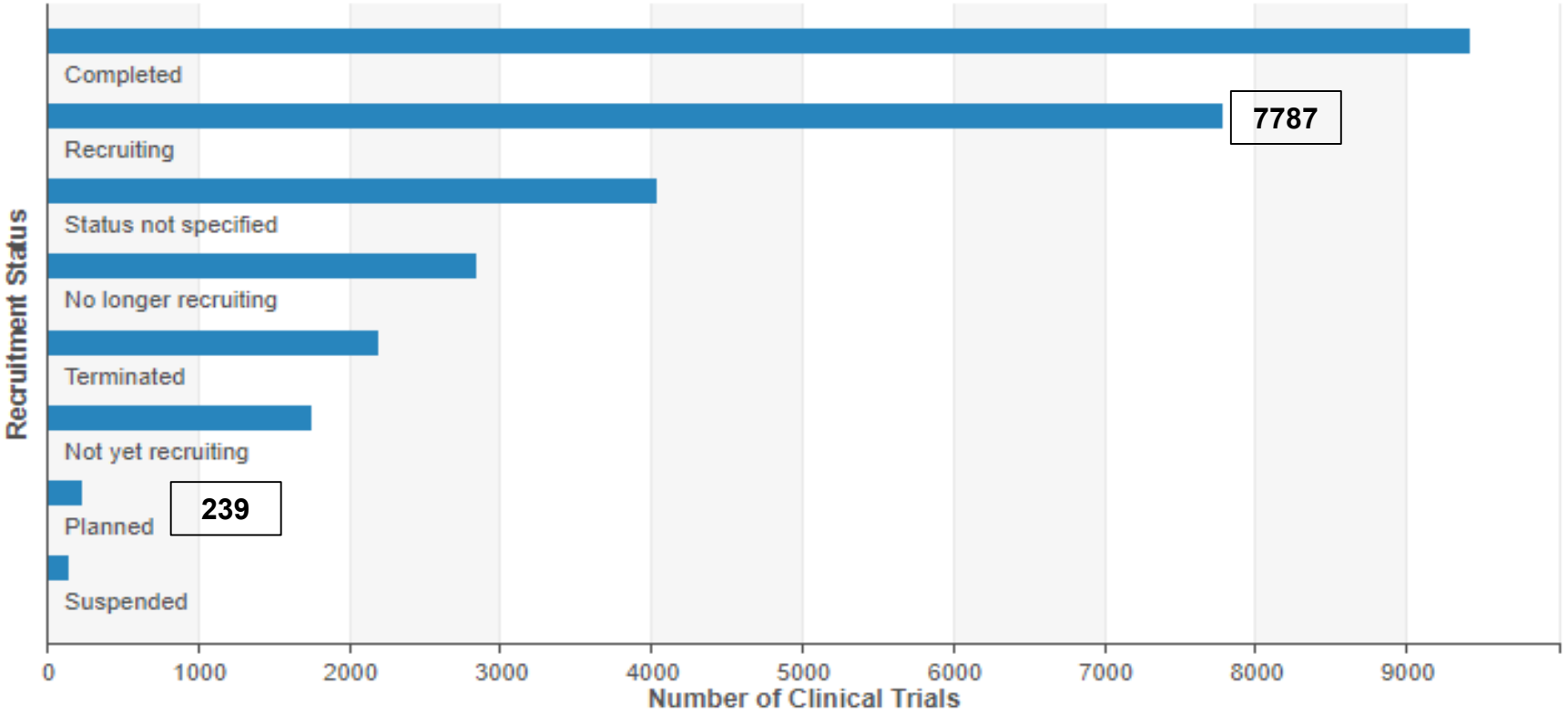
So What Does That Mean in The Rare Disease Space?

- Analyze trial design across the entire rare disease space
- Understand which rare diseases have the most competition for indication prioritization
- Break down trial timelines, recruitment rates, and endpoint completion dates for individual rare diseases and granular patient segments
- See how the use of biomarkers in rare diseases have affected trial success
- Analyze patient segmentation to understand:
    - How it affects recruitment timelines and rates
    - Where your competitors are recruiting the same patient segment
    - Which sites have experience not only in the rare diseases you are interested in, but also in enrolling the patients you need

Recruitment Status



Track the status of all rare disease trials, or narrow it down to specific diseases. Set up alerts so that you always know what your competitors are up to and let Cortellis do the leg work for you. In the increasingly competitive rare disease space you can't afford to be a step behind.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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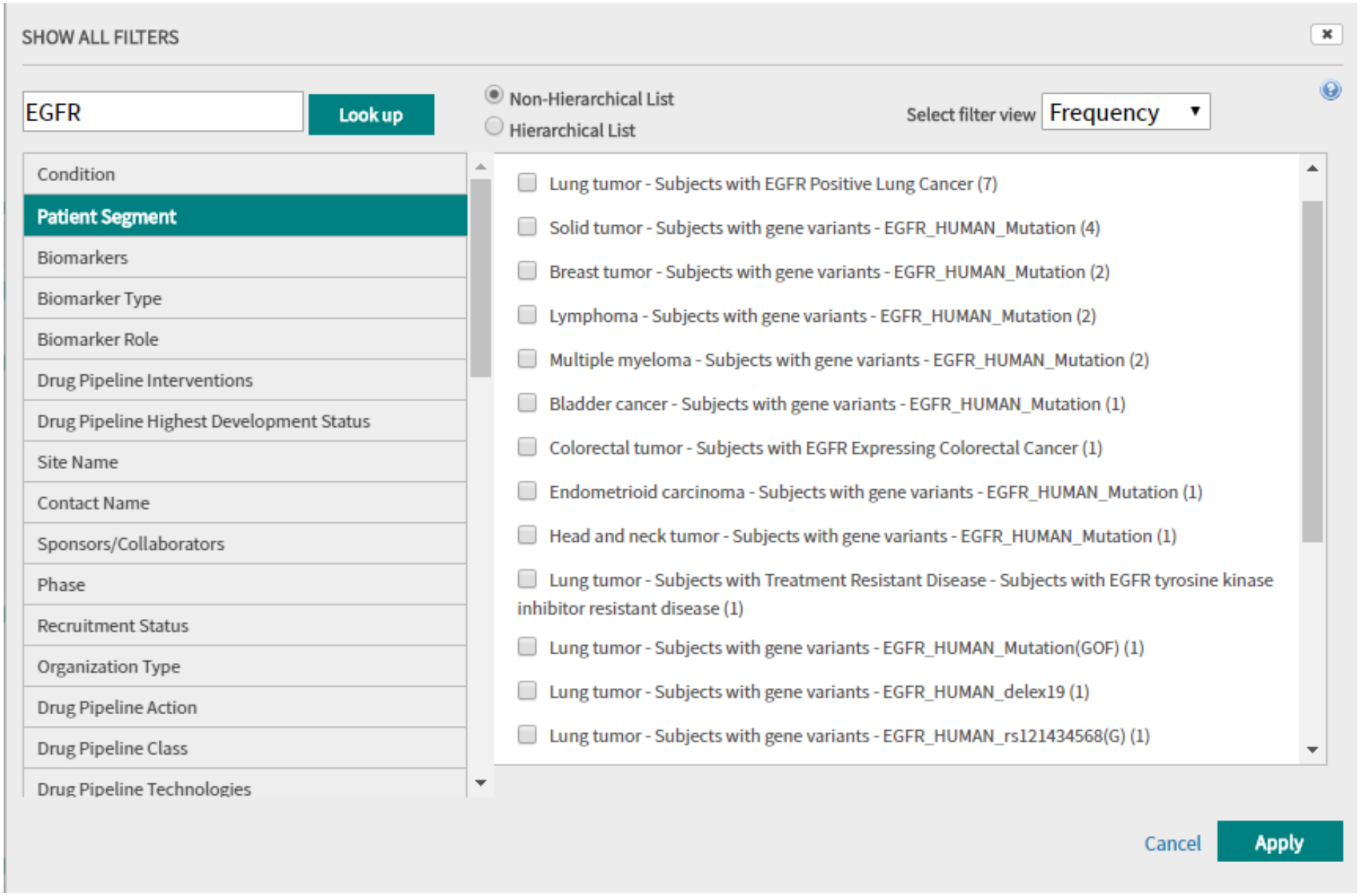

Analyze particular patients down to the gene variant level and see what indications they are linked to.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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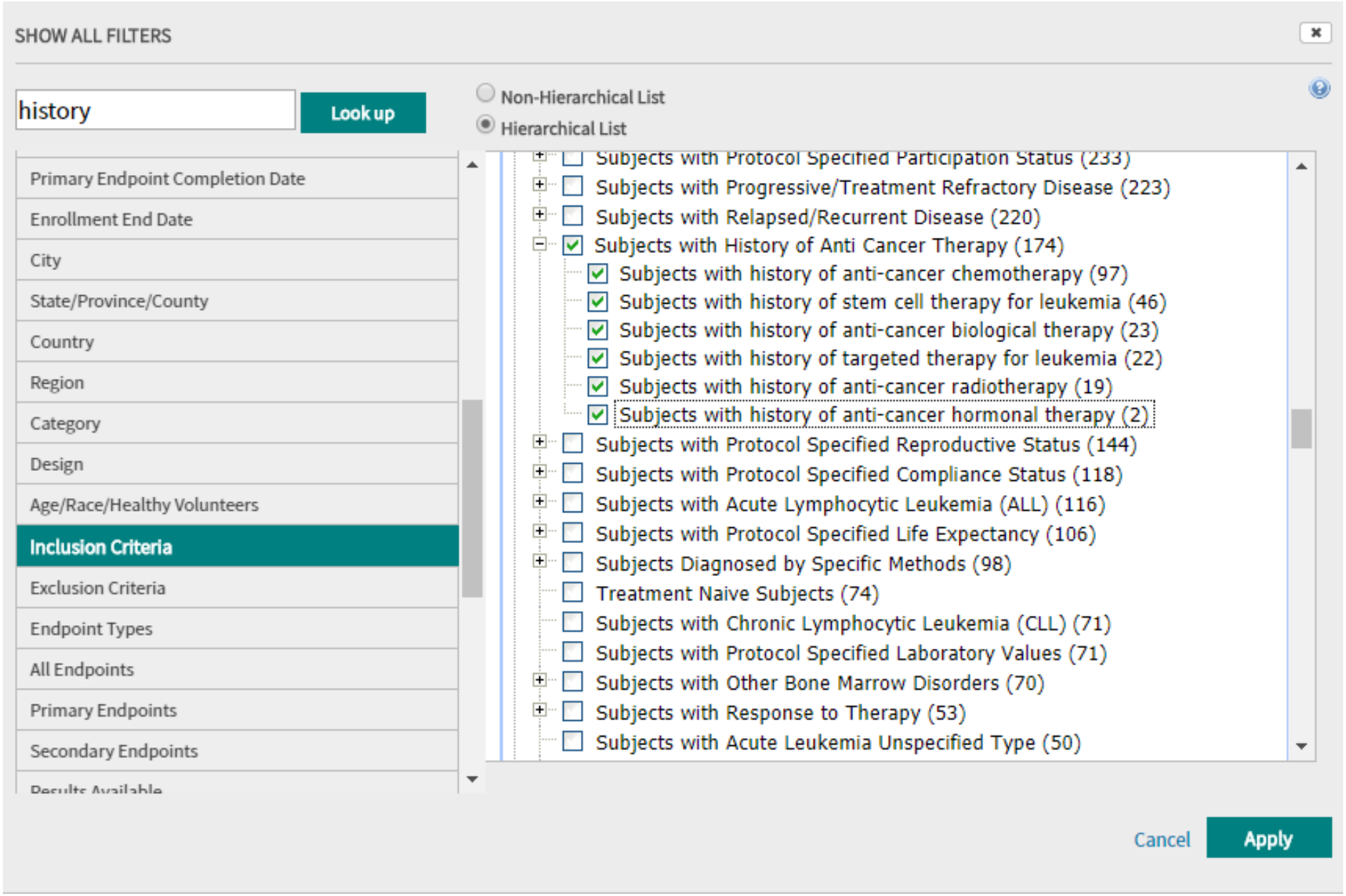

Distinguish between lines of therapy for individual therapies

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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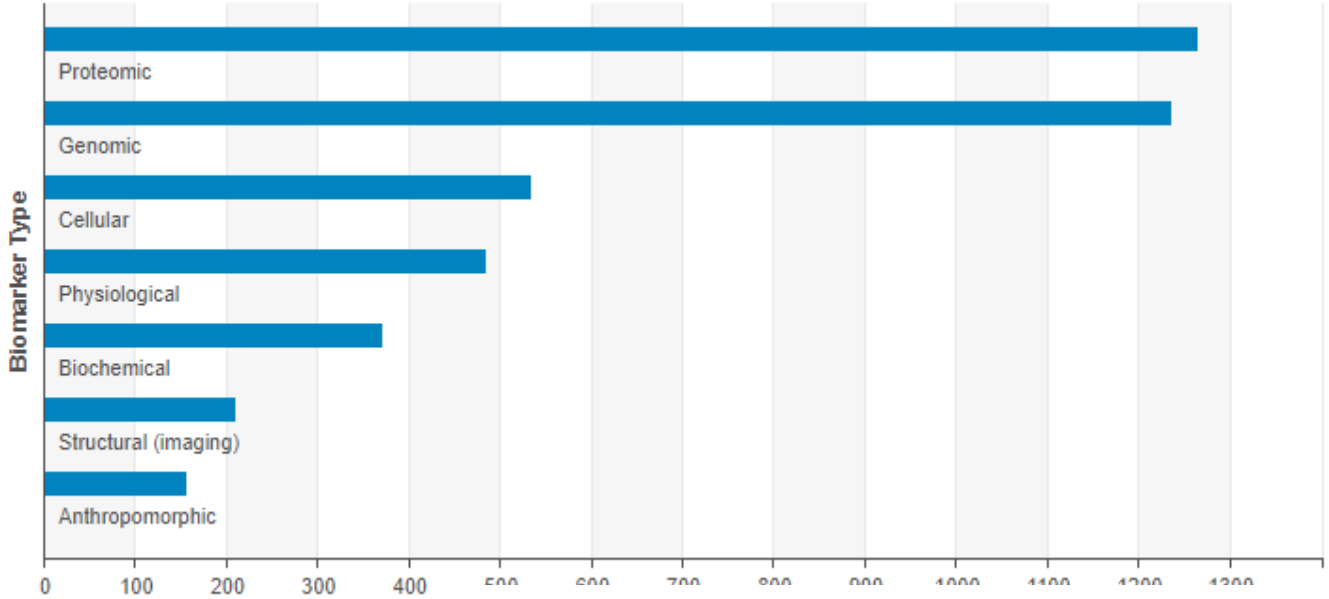
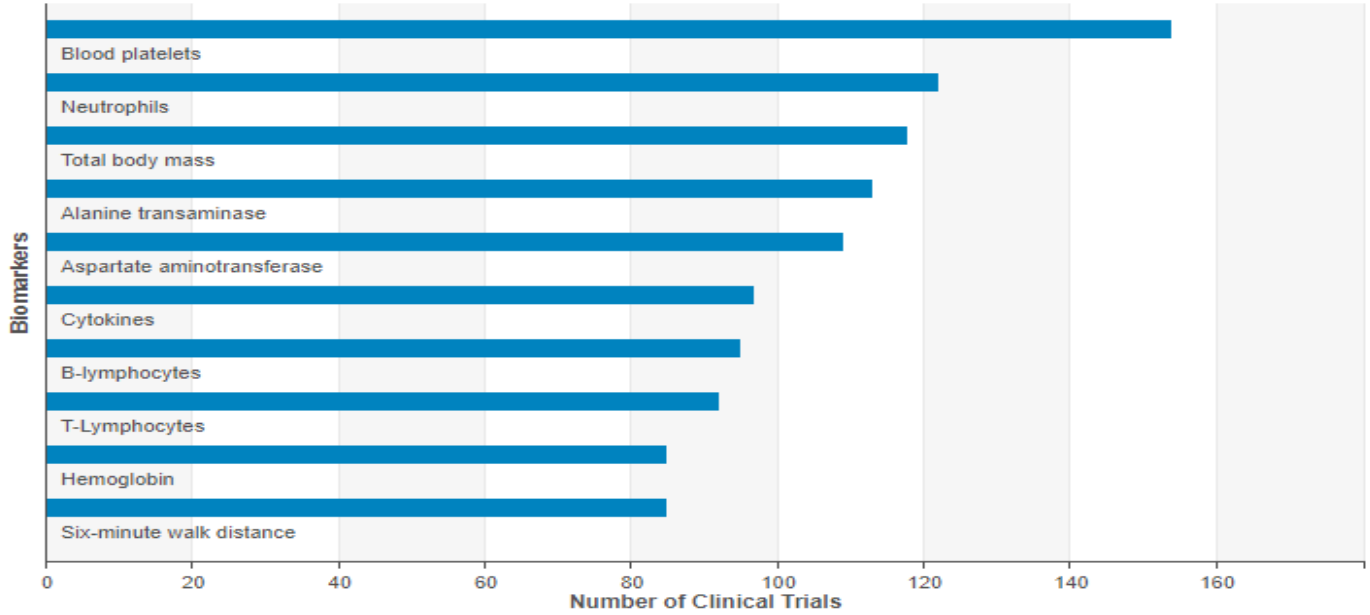


See what types of biomarkers are being studied most in the rare disease space…



And what those individual biomarkers are.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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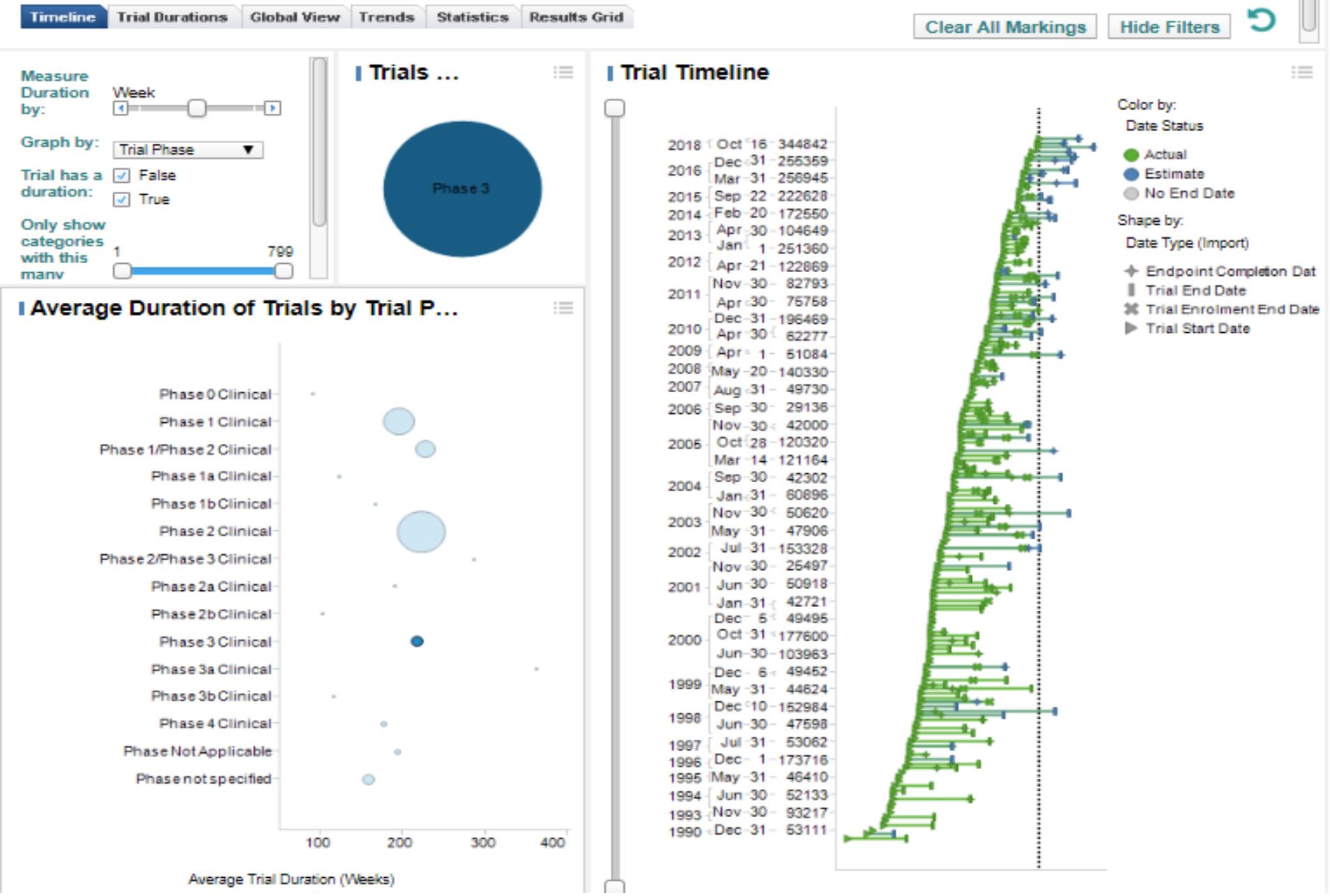
Using the built in timeline analytics shown on the next slide you can;

- Gain a rapid overview of competitive programs in your area to ensure that your program has maximal opportunity to be first to market or inform the Clinical Development teams of possible threats that will require you to demonstrate greater efficacy than previously launched therapies.

- Understand how competing programs may influence your strategic decisions relating to trial design and patient segmentation.

- Create a timeline of trials active against the same clinical criteria as you.

- Insight into actual and estimated trial durations to enhance your trial feasibility analysis and trial execution to reduce risks related to slow patient enrolment.



Data shown is for all Non-Hodgkin Lymphoma trials. Filters are applied to limit the trials to phase 3.

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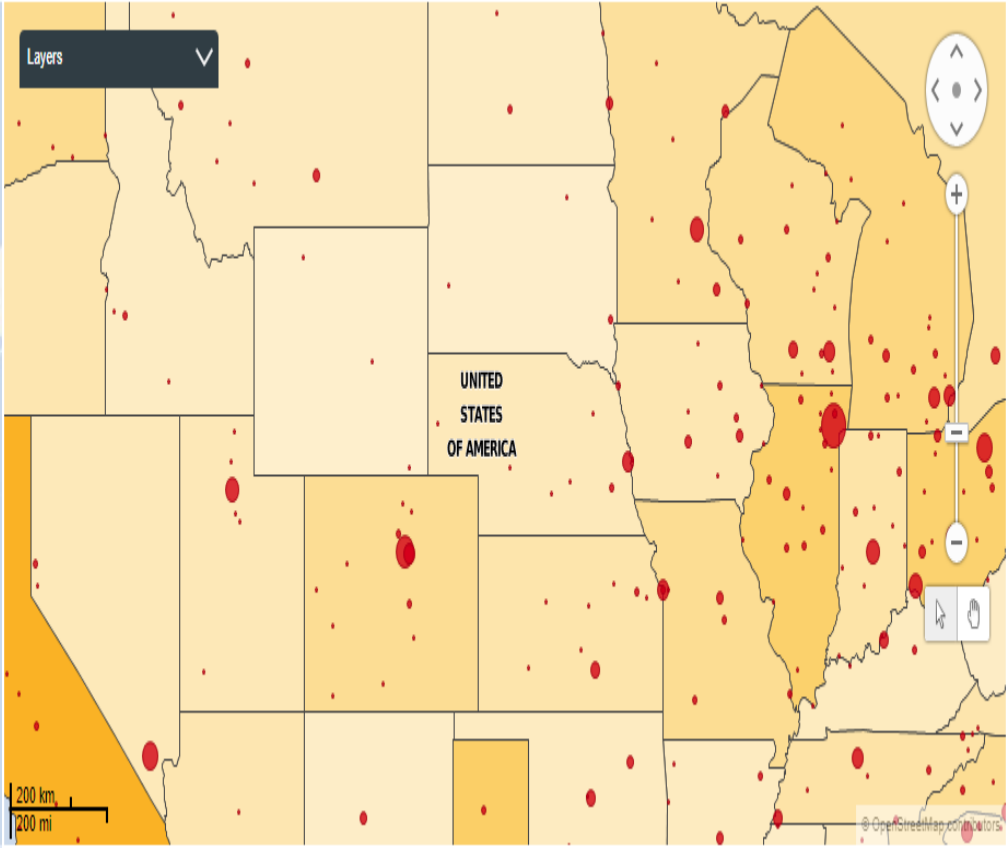
Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence



The power of Cortellis to take site selection to the granular patient segment level is unparalleled. Analyze rare diseases from a global perspective to find the right sites who can enroll the patients you need and understand where your highest competition will be.

City	Postal Code	Site Main Name	Closed Trials	Ongoing Trials	Unknown Trials
		Sherman Hospital	2	---	---
Elmhurst	60126	Elmhurst Memorial Hospital	2	---	---
Eureka	61530	Eureka Community Hospital	7	---	---
		Eureka Hospital	4	1	---
		Illinois CancerCare-Eureka	8	1	---
Evanston	60201	Evanston CCOP-NorthShore University H...	1	---	---

Eureka Hospital

Heat Map reflects rare disease trials with start date of 2008-2010. Data includes all completed, ongoing, and terminated/suspended trials.

Source: Clarivate Analytics, Cortellis Clinical Trials Intelligence

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Questions

To learn more go to: Clarivate.com/Cortellis

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