Program Topic

- Exploring patient enrichment, patient centricity and a forward discussion in oncology trials to maintain a patient-centric approach
- Discussing strategies to design clinical trials to enrich for target patient populations
- Evaluating the true statistics of patient participation in clinical trials
- Facilitating availability while protecting patient safety and avoiding interference with drug development
- Speculating on industry’s role in expanded access programs

Disclosure

The views expressed in this presentation are those of the presenter, and are not necessarily the views of Kezar Life Sciences and/or its partners.

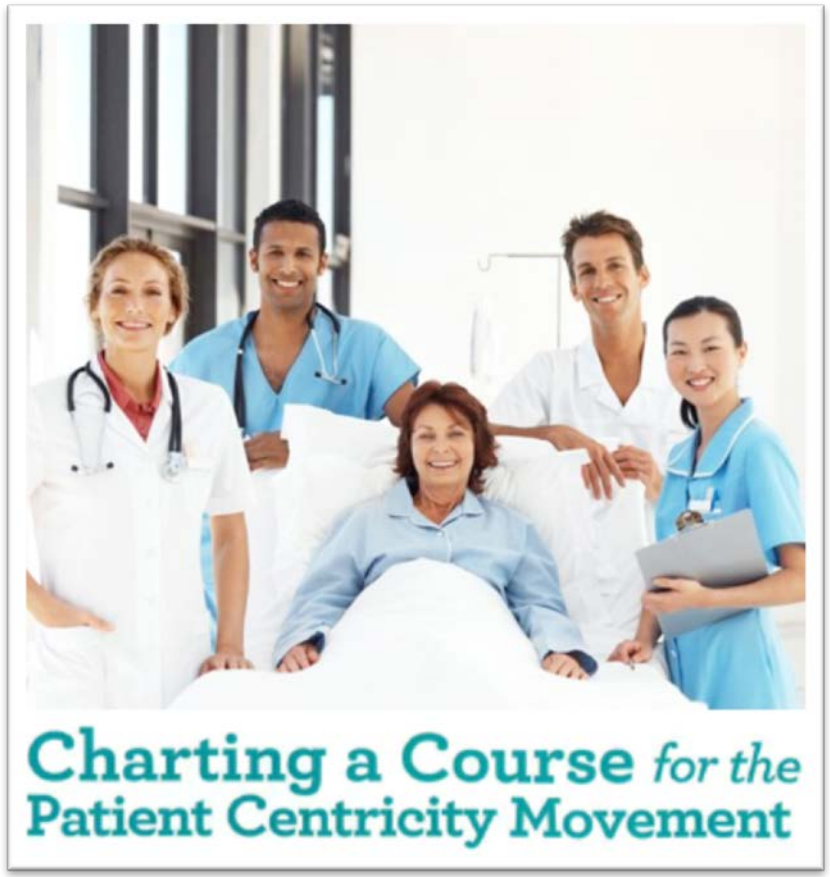
A Question to Sponsors:

Have we gone too far?

Jennifer Brandl
Clinical Trial Manager
Kezar Life Sciences

A Patient Centric Movement

Patient Centric Approaches



- **Digital patient**
- **Early stage involvement**
- **Protocol design**
- **Communication channels**
- **Patient engagement**
- **Patient stakeholders**
- **Data transparency**
- **Technology**

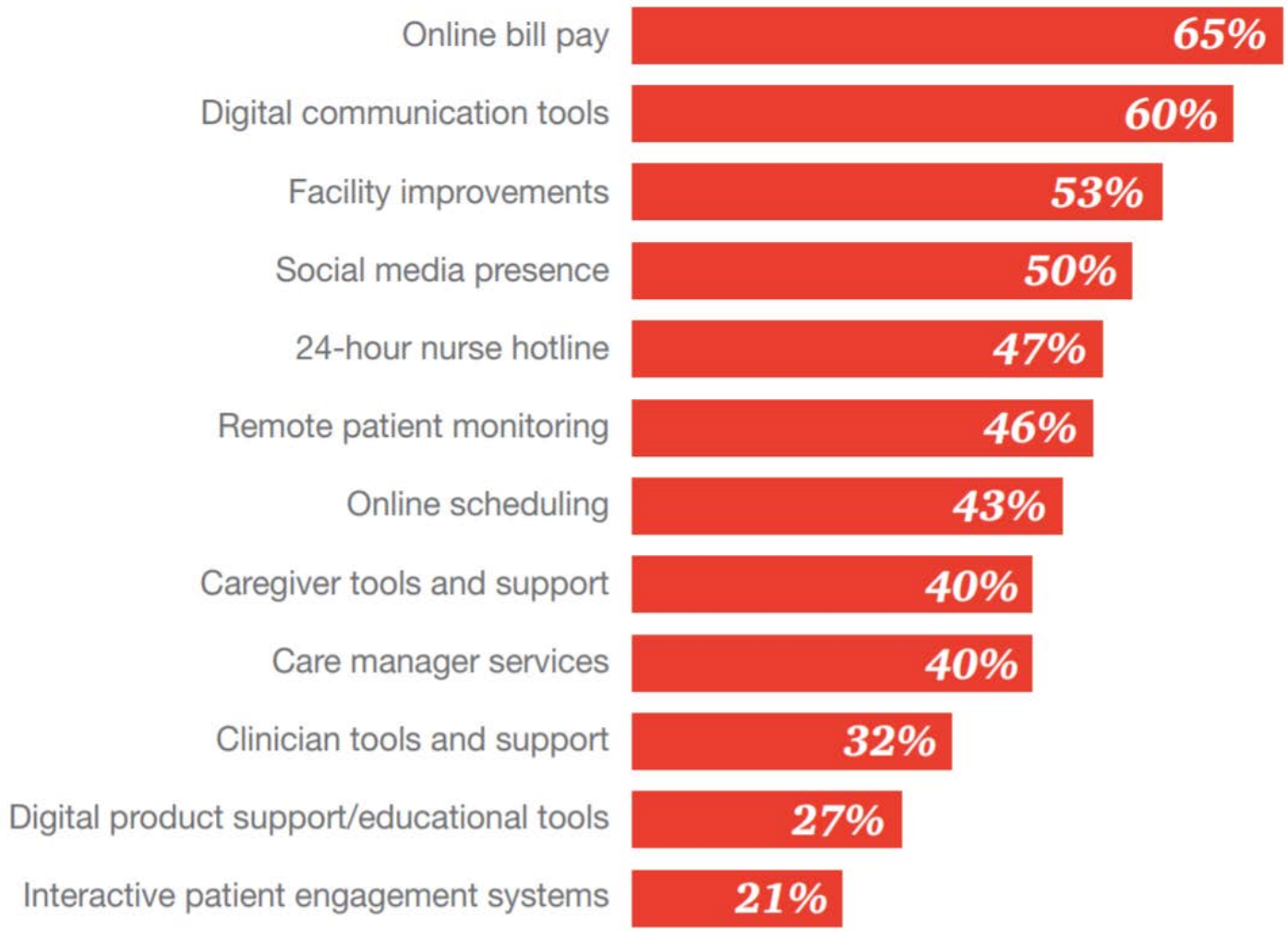
Source : Sharma NS. Patient centric approach for clinical trials: Current trend and new opportunities. *Perspectives in Clinical Research*. 2015; 6(3):134-138.

Focused on Patient Centricity

POLL

How many of you have been involved in patient centric initiatives or approaches?

Healthcare Providers are Investing in Services

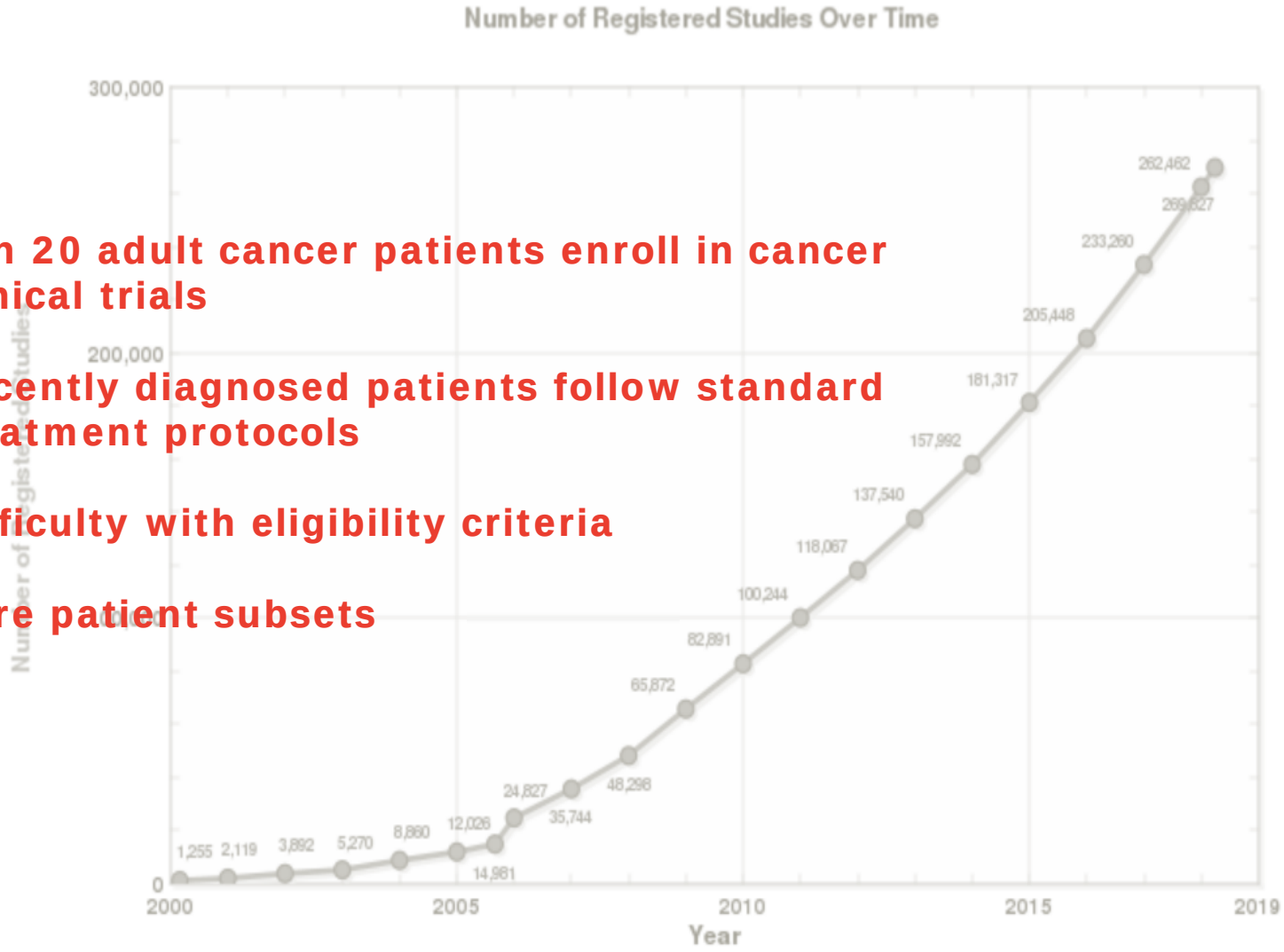


Source : PwC Health Research Institute Provider Executive Survey 2017

Impact vs. Reality

Patient Enrollment in Oncology Trials

- **1 in 20 adult cancer patients enroll in cancer clinical trials**
- **Recently diagnosed patients follow standard treatment protocols**
- **Difficulty with eligibility criteria**
- **Rare patient subsets**



Source : https.//clinicaltrials.gov; American Society of Clinical Oncology Educational Book;
Institute of Medicine (US) Forum on Drug Discovery, Development, and Translation

Patient Enrichment and Study Design

Huge focus is given to clinical trial design and patient enrichment. Those who conduct clinical trials "enrich" study populations to identify a population of patients in whom a drug effect is more likely to be demonstrable.

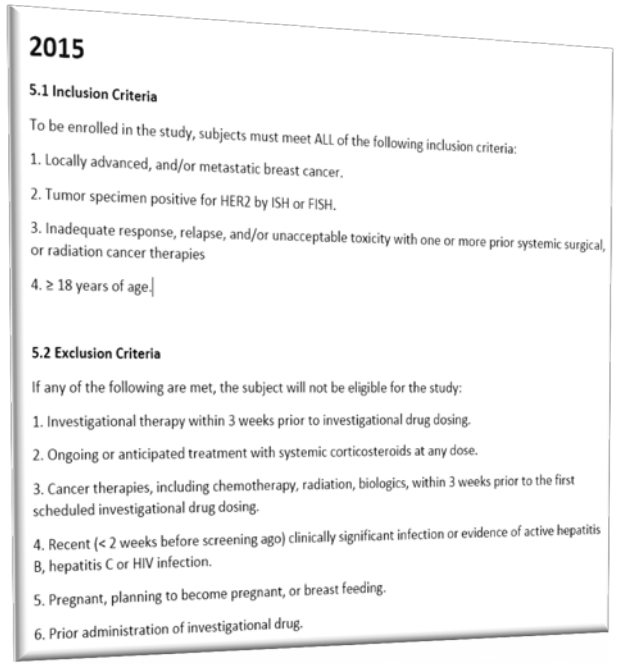
- Prospective use of patient characteristics
- High risk population
- Population that will detect a drug effect
- Eliminate patients like to lead to early death
- Omit due to genetic characteristics
- Select based on pathophysiology
- Marker-positive and marker negative groups
- Randomized withdrawal

Adaptive

Targeted

Reduced cost

Company X



2015

5.1 Inclusion Criteria

To be enrolled in the study, subjects must meet ALL of the following inclusion criteria:

1. Locally advanced, and/or metastatic breast cancer.

2. Tumor specimen positive for HER2 by ISH or FISH.

3. Inadequate response, relapse, and/or unacceptable toxicity with one or more prior systemic surgical, or radiation cancer therapies

4. ≥ 18 years of age.

5.2 Exclusion Criteria

If any of the following are met, the subject will not be eligible for the study:

1. Investigational therapy within 3 weeks prior to investigational drug dosing.

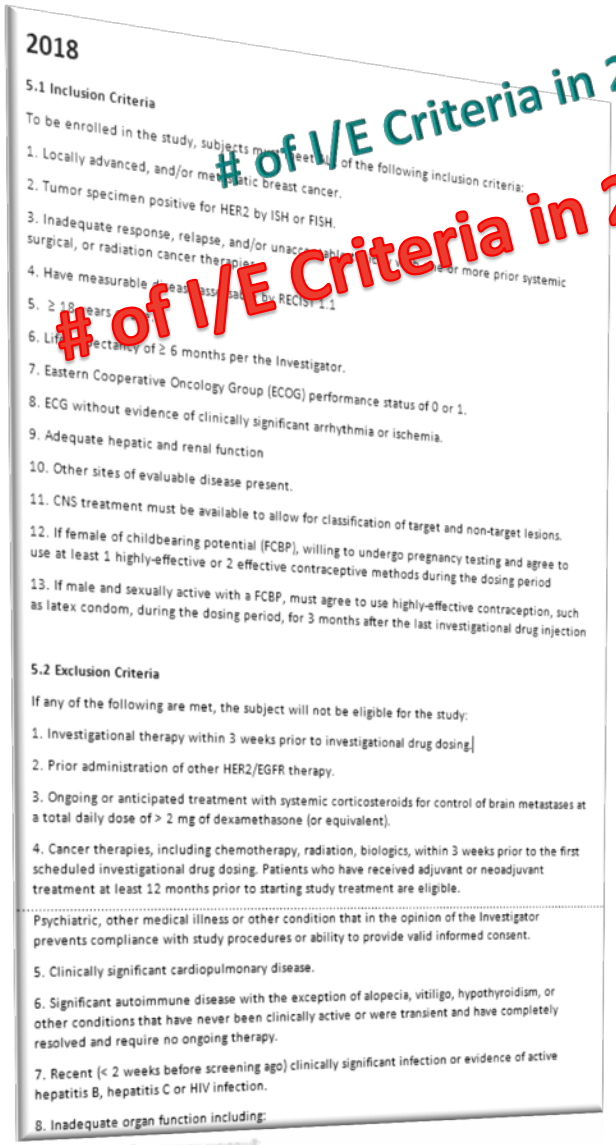
2. Ongoing or anticipated treatment with systemic corticosteroids at any dose.

3. Cancer therapies, including chemotherapy, radiation, biologics, within 3 weeks prior to the first scheduled investigational drug dosing.

4. Recent (< 2 weeks before screening ago) clinically significant infection or evidence of active hepatitis B, hepatitis C or HIV infection.

5. Pregnant, planning to become pregnant, or breast feeding.

6. Prior administration of investigational drug.



2018

5.1 Inclusion Criteria

To be enrolled in the study, subjects must meet ALL of the following inclusion criteria:

1. Locally advanced, and/or metastatic breast cancer.

2. Tumor specimen positive for HER2 by ISH or FISH.

3. Inadequate response, relapse, and/or unacceptable toxicity with one or more prior systemic surgical, or radiation cancer therapies

4. Have measurable disease assessed by RECIST 1.1

5. ≥ 18 years of age.

6. Life expectancy of ≥ 6 months per the Investigator.

7. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

8. ECG without evidence of clinically significant arrhythmia or ischemia.

9. Adequate hepatic and renal function

10. Other sites of evaluable disease present.

11. CNS treatment must be available to allow for classification of target and non-target lesions.

12. If female of childbearing potential (FCBP), willing to undergo pregnancy testing and agree to use at least 1 highly-effective or 2 effective contraceptive methods during the dosing period

13. If male and sexually active with a FCBP, must agree to use highly-effective contraception, such as latex condom, during the dosing period, for 3 months after the last investigational drug injection

5.2 Exclusion Criteria

If any of the following are met, the subject will not be eligible for the study:

1. Investigational therapy within 3 weeks prior to investigational drug dosing.

2. Prior administration of other HER2/EGFR therapy.

3. Ongoing or anticipated treatment with systemic corticosteroids for control of brain metastases at a total daily dose of > 2 mg of dexamethasone (or equivalent).

4. Cancer therapies, including chemotherapy, radiation, biologics, within 3 weeks prior to the first scheduled investigational drug dosing. Patients who have received adjuvant or neoadjuvant treatment at least 12 months prior to starting study treatment are eligible.

Psychiatric, other medical illness or other condition that in the opinion of the Investigator prevents compliance with study procedures or ability to provide valid informed consent.

5. Clinically significant cardiopulmonary disease.

6. Significant autoimmune disease with the exception of alopecia, vitiligo, hypothyroidism, or other conditions that have never been clinically active or were transient and have completely resolved and require no ongoing therapy.

7. Recent (< 2 weeks before screening ago) clinically significant infection or evidence of active hepatitis B, hepatitis C or HIV infection.

8. Inadequate organ function including:

# of I/E Criteria in 2015: 10

# of I/E Criteria in 2018: 37

Post Market Approval

What options are out there?

- **Advisory Boards**
- **Advocacy Groups**
- **What about Expanded Access?**

POLL

How many of you know about Expanded Access?

Expanded Access Programs

"They strike a balance between pre-approval access and patient safety."

"They are too restrictive and do not facilitate enough access to patients with unmet medical needs."

"Requests by patients and physicians for access to drugs will increase."

"Slow approvals, advocacy, niche populations and greater awareness are driving the expected increase in demand."

"Enrollment will compete with ongoing trials."

"Fulfillment of unmet patient needs in an ethical way."

Source : Clinigen Survey 2015

Expanded Access Benefits and Overview

Mechanism to provide a reactive means for individual patients to access to treatment not yet approved by regulatory authorities

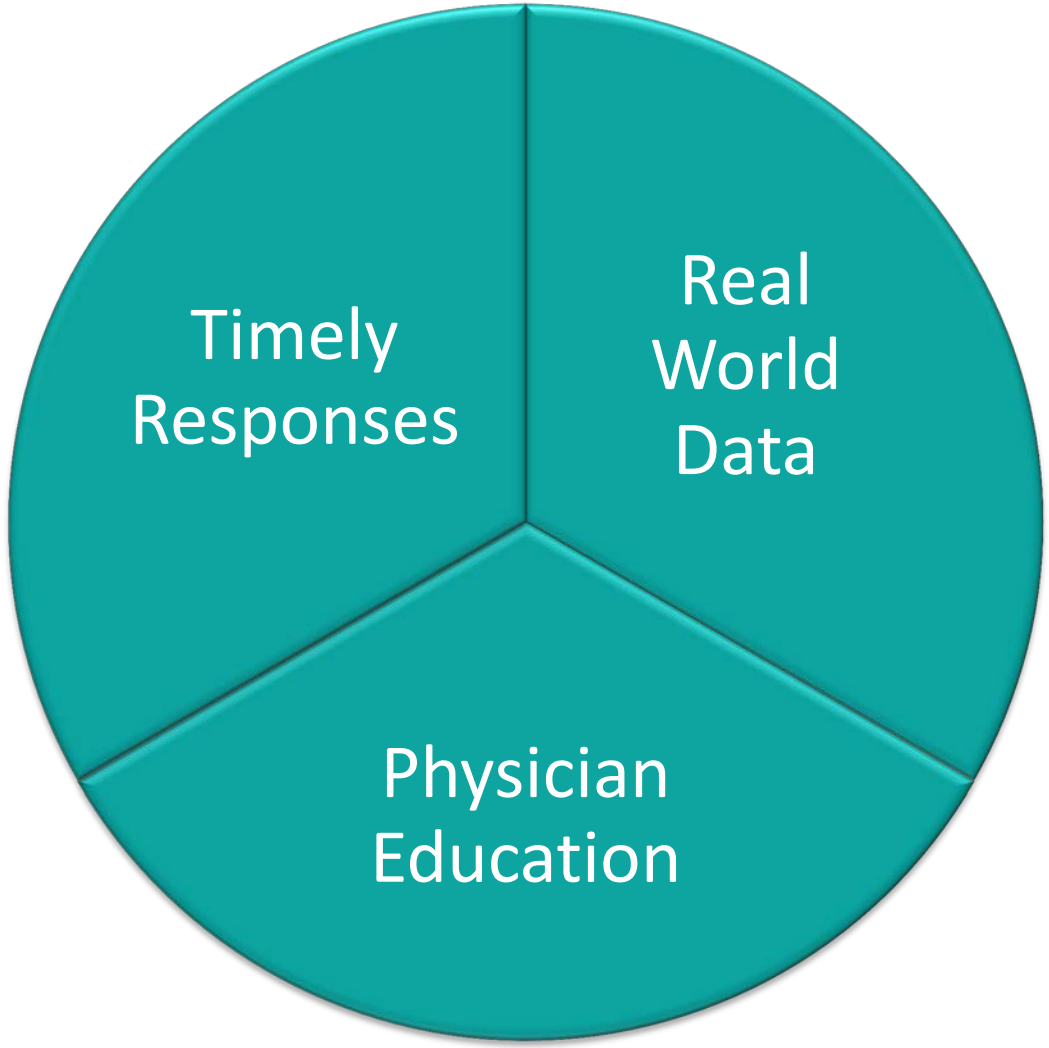
- Compassionate use programs (CUPs) and early access programs
- Include Name Patient Use, Group/Cohort
- Sufficient evidence of safety and effectiveness
- Enrollment cannot compete with going clinical trials
- Provide great access during approval process in various countries
- Develop network of physicians who have experience with the treatment
- Generate additional review to support product development
- Avoid perception of being a “seeding study”

21st Century Cures Act

Manufacturers or distributors of an investigational drug SHALL make publically available their policy on evaluating and responding to Expanded Access Requests

Source : U.S. Food and Drug Administration; MK&A

Big Pharma Harmonization



Vendors and Clinical Trial Supply Companies

Data Collection

- Observational data collection, wearables mHealth
- Analysis of Real World Data (RWD)
- Genetic testing databases

Supply Chain Solutions

- Comparator sourcing, labeling, biosimilar services
- Medical adherence solutions, continuous patient monitoring

Program Support

- Policy creation, implementation and program scoping
- Feasibility, program design
- Engagement plan

A Question to Sponsors

Maybe we haven’t gone far enough…

Questions