Intersecting opportunities and remaining challenges in developing nervous system drugs.

### CHALLENGES*

- **Lack of understanding of underlying cellular mechanisms of disease**
  - Difficulty in recapitulating complex disease processes in vitro.
- **High failure rates following large financial investments**
  - Many preclinical models do not match specific endpoints.
- **Uncertainty and complexity of regulatory requirements and processes**
  - Clarity of regulatory agency requirements.
- **Increased regulatory burden**
  - Clarity of regulatory agency requirements.
- **Resource constraints**
  - Insufficient capacity to develop and test hypotheses.
- **Insufficient knowledge of disease models**
  - Inability to develop preclinical models.
- **Deficiencies in translational research**
  - Lack of mechanisms to measure biological criteria and therapeutic effects.
- **Data sharing**
  - Lack of sharing and reproducibility.
- **Clinical biomarker validity and reproducibility**
  - Lack of homogeneity and complexity.
- **Clarity of regulatory agency requirements and processes**
  - Insufficient knowledge of regulatory concepts.
- **Uncertainty and complexity of regulatory requirements and processes**
  - Clarity of regulatory agency requirements.
- **Insufficient knowledge of disease models**
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### OPPORTUNITIES*

- **Utilize combinations of animal and endophenotype models**
  - Use of imaging techniques to identify disease-associated endpoints.
- **Strategies to use animal data to inform patient stratification**
  - Use of imaging techniques to identify disease-associated endpoints.
- **Increased availability of new and emerging technologies**
  - Use of imaging techniques to identify disease-associated endpoints.
- **New data resources for human neurology**
  - Use of imaging techniques to identify disease-associated endpoints.
- **Improved preclinical study standards**
  - Use of imaging techniques to identify disease-associated endpoints.
- **Improved pharmaceutical study standards**
  - Use of imaging techniques to identify disease-associated endpoints.
- **Data sharing**
  - Lack of sharing and reproducibility.
- **Clinical biomarker validity and reproducibility**
  - Lack of homogeneity and complexity.
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- **Clinical biomarker validity and reproducibility**
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**NOTE:** The graphic illustrates common challenges and opportunities suggested by individual participants at workshops hosted by the IOM Forum on Neuroscience and Nervous System Disorders (Accelerating Therapeutic Development for Nervous System Disorders Towards First-in-Human Trials [April 8-9, 2013] and Improving Translation of Animal Models for Nervous System Disorders Towards First-in-Human Trials [April 8-9, 2013]). Statements, recommendations, and opinions expressed are those of the individual participants and are not necessarily endorsed or verified by the IOM, and should not be construed as reflecting any group consensus.

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**Figure:**

- **DRUG DEVELOPMENT PIPELINE**
  - **CHALLENGES:**
    - Lack of understanding of underlying cellular mechanisms of disease
    - High failure rates following large financial investments
    - Uncertainty and complexity of regulatory requirements and processes
    - Insufficient knowledge of disease models
    - Deficiencies in translational research
    - Data sharing
  - **OPPORTUNITIES:**
    - Utilize combinations of animal and endophenotype models
    - Strategies to use animal data to inform patient stratification
    - Increased availability of new and emerging technologies
    - New data resources for human neurology
    - Improved preclinical study standards
    - Improved pharmaceutical study standards

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**Forum on Neuroscience and Nervous System Disorders**

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