



HORIZONS

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26-28 March 2008 • San Francisco

Time to Market Planning for a New Chemical Entity (NCE) NDA Submission: Nonclinical/Clinical




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Agenda

- Define the goal
- Minimize cost with a targeted approach
- Ensure datasets are linked correctly to enable continuous development
- Regulatory strategies/options
- Obtain consensus on strategies to minimize risk



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What's the Goal?

- NDA Submission
- NDA Filing
- NDA Approval
- Considerations
 - Data exclusivity
 - PDUFA timelines
 - Business strategies

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Targeted Approach

- Target product profile
- Acceptable safety
- Competitor information/Prior approvals
- Standard of Care
- Biomarkers

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Target Product Profile

- Summary of the drug development program plan
- Summary of drug labeling concepts
- Working/living document
- Not public information
- See guidance for template

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How is the TPP generated?

- SBAR summary basis of approval
- EPAR European public assessment reports
- Competitor labels
- Advisory Committee meetings/minutes
- Combination of business and medicine

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Acceptable Safety

- Risk versus benefit assessment
- Consider the patient population
- Alternate therapies?
- Monitor?
- Control?
- Human safety is the criteria!

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Standard of Care

- Standard of care \neq Latest drug approval
- Needs to be negotiated
- Not a marketing decision
- Requires discussion with FDA
- Requires FDA agreement
- Consider alternate options

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Biomarkers

- Great historical examples
- Potential for targeted population
- Will require additional submissions or product approvals
- Potential for surrogate endpoints
- Will require validation

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Regulatory Strategies

- Holistic approach
- Get back to the goal
- Data guide the drug development
- Data guide the FDA negotiations
- Consider options

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Nonclinical and Clinical link

- Building a safety package
- Consider the patient population (ICH versus Oncology)
- Timing of DART studies
- Chronic administration?
- ADME profile
- Impurity profiles
- What can't be repeated

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Clinical Pharmacology/Nonclinical link

- Again, building a safety package
- Don't forget the TPP
- Clearly define requirements for continued development

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ClinPharm/Clinical link

- When is data required?
- What can be included in pivotal trials?
- Ideally complete prior to phase 3

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Nonclinical/Clinical/CMC link

- Consider timing of major manufacturing changes
- Ensure safety data covers commercial material
- Commercial material in Clinical studies?
- Development to Commercial trigger

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Regulatory Strategies

- Orphan drug approach
- Accelerated approval
- Fast track
- Expedited review
- Pre-submission
- Subpart H/Subpart E
- Special protocol assessment

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Orphan Drug Status

- Consider resource load
- Data exclusivity
- Timing
- Potential for funding

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Accelerated Approval

- Subpart H
- Established surrogate endpoint
- Validated surrogate endpoint
- Usually other than survival or irreversible morbidity
- Applies to study design

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Fast Track Designation

- Originated in FDAMA 1997
- Aid the development of products intended to address unmet medical needs for serious and life threatening conditions
- Subpart E
- Expedited /Accelerated Development

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Priority Review

- Discuss at Pre-NDA meeting
- Request at filing
- Timeline compresses both parties
- Advisory committee preparation
- Coincides with early launch
- Global impact

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Special Protocol Assessment

- Three protocols qualify
 - Animal carcinogenicity
 - Final product stability
 - Phase 3 protocols to support efficacy claims discussed at an EOP2 meeting
- 45 day evaluation
- May include advisory committees
- Follow up meetings are type A

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FDA Interactions

- Pre-IND
- EOP1
- EOP2
- Pre-NDA

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Pre-IND Meeting

- 6 months prior to IND filing
- Not an entitlement meeting
- Nonclinical study design
- Clinical study design
- Review safety monitoring

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End of Phase 2 Meeting

- 6 months prior to phase 3 trials
- Safety package
- Clinpharm package
- Tox/ADME studies
- Phase 3 clinical study design
- TPP

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Pre-NDA Meeting

- 6 months prior to submission
- Acceptance of data
- Labeling/TPP
- Safety concerns
- Filing logistics

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Conclusions

- Integration of a regulatory strategy with the business, marketing and clinical development strategy are key to success
- There are many regulatory options that need to be negotiated with FDA based on data and goals



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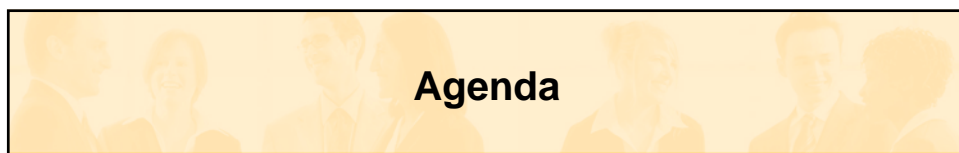
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**Time to Market Planning for a New Chemical
Entity (NCE) NDA Submission:
Nonclinical/Clinical**

**Gretchen Bowker, RAC
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Thank You!

Questions???

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