



Early Phase Clinical Trials: *Opportunities for Australasian Biotech Companies from the Regulatory Perspective*

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Topics to be Discussed

1. Leveraging limited resources and regulatory intelligence to support clinical development
2. Being small AND regulatory smart
3. Learning lessons (often from others)



Top 5 Encountered Clinical Issues

1. Lack of overall clinical development plan, including requirements for future registration
 - Not ensuring that the approach is compatible with international practice
2. Lack of draft product labelling as a steering tool for clinical development
3. Inadequate discussion of appropriate early-stage clinical studies with regulators in key regions
4. Not utilising the appropriate comparator in clinical studies
5. Inadequate definition of the product at each stage of development



Avoiding Risk in Early Phase Trials

To address the potential deficiencies that could arise:

- Develop a comprehensive regulatory strategy and clinical development plan at an early stage
- Validate the clinical development plan by meeting with regulators in concerned regions



Regulatory and Clinical Strategy

- Consider all aspects of development
 - Quality, nonclinical and clinical
 - How are they connected?
- **Use regulatory intelligence**
 - Identify specific regulatory requirements for the product in various regions
- Apply high standards of record keeping and document control – start today!



Case Study 1

A small company had a monoclonal antibody product for the treatment of Stage IIa - IV melanoma

- The company had an open IND in the US, had obtained Orphan designation, and completed a Phase I (patient) study
- A partner will fund the Phase II/III trials if the required approvals can be obtained in EU countries for the Clinical Trial Applications, and the product is designated Orphan in the EU
- Clinical material for Phase I was sourced from Taiwan

Problems encountered:

- Designation for Orphan status in the EU may be different to that in the US, especially where subpopulations of patients are involved
- Requirements for GMP for clinical trial products are strict in the EU



Formulate and Validate the Strategy

Prepare draft labelling to define the program goals for the product, then meet with international regulatory agencies (particularly in Europe and the US FDA) to help validate the developmental program and avoid unexpected problems

Result

- Will facilitate progress from nonclinical to clinical phase
- Will help avoid unnecessary backward steps
- Should add value to the program for potential investors



Leverage Use of Resources

- Minutes of scientific advice meetings serve to document progress and further regulatory requirements (**crucial** in due diligence)
- Meetings available to biotech companies
 - US FDA has defined scheme for (**free**) meetings (“pre-IND” etc)
 - Face-to-Face (**free**) consultations with the TGA
 - Face-to-face meetings with EU Member State agencies. Cost is between **EUR 5,000-7,000**.
 - Formal scientific advice (**EUR 70,000 / 7,000 for SME**) through EMEA / SAWP.



Case Study 2

A New Zealand company is developing a recombinant protein product for the treatment of small cell lung cancer

- Successful completion of Phase IIa study in Australia under CTN
- Licensee interested to move the product into a Phase IIb/III pivotal studies performed due diligence, enlisting the help of international regulatory and clinical specialists among others
- Significant deficiencies found in both quality (e.g. lack of validated bioassay) and nonclinical (e.g. no immunogenicity assay, protein is highly conserved) data, impacting the timeline to the next clinical trial
- Deal is made but is dramatically de-valued by these deficiencies



Case Study 2 (cont)

Lessons

- What went wrong?
 - Rushing through initial development without consolidating information - costing more later on and de-valuing the program
- What could have been done to minimise these risks?
 - A comprehensive documentation review in light of EU and US regulatory expectations - the final target audience
 - Validation through agency interaction – identify and correct “hot spot” problems before post-Phase II lockdown to avoid massive comparability issues
- Remember what the CTN process entails (and what it does not) – be regulatory intelligent



Follow Advice given by Regulators!

- Approach regulators with a thoughtful program
- Ask relevant questions to obtain relevant answers
- Advice is given to help and guide the Company – don't hide what you consider to be “problems”
 - These will likely surface later and strip value from your program
- Minutes from agency meetings are recorded and available at a later date
 - Advice provided at consultation meetings is not binding, but should be followed unless there is compelling justification
 - Advice from regulators can validate your program strategy and **ADD VALUE**



Thank you!



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