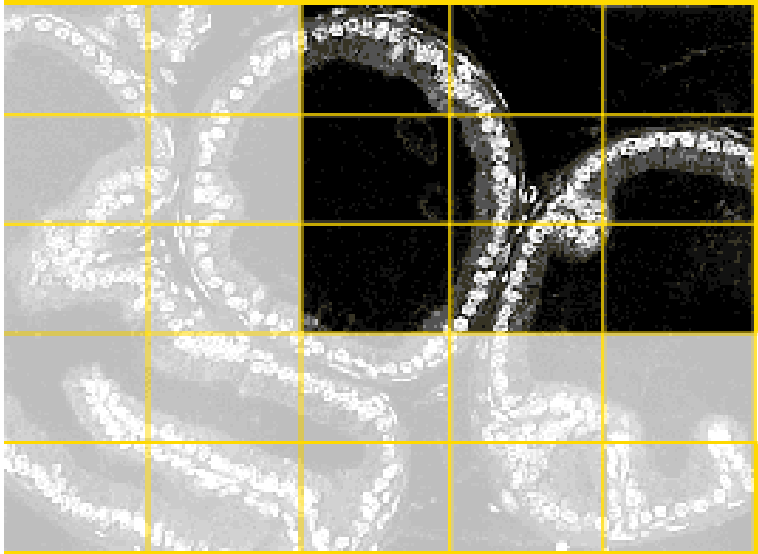
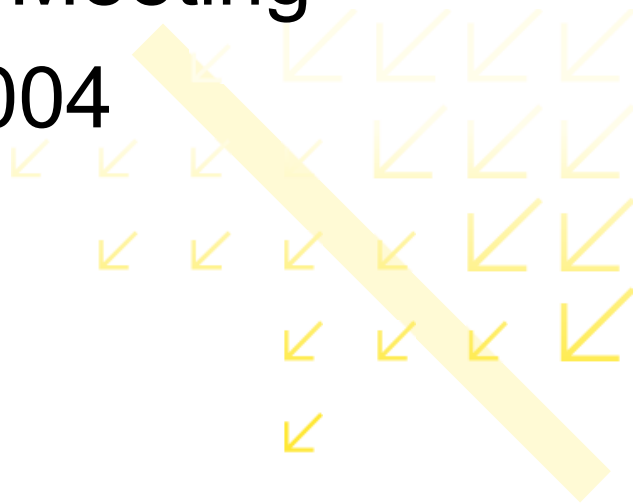


# Marshall Edwards Inc

# Marshall Edwards Inc

## Annual Shareholders Meeting

## 16 December 2004



- Nasdaq National Market and the London Alternative Investment Market
- Nasdaq IPO Dec 2003

- Stock issued : 1 Unit at *$7.50* (1 Share / 1 Warrant)
  3X oversubscribed
  priced over indicated range

- Stock price now :1Share at $9 / 1 Warrant at $5 to equal 1 Unit at *$14*
  2.4 million warrants issued at $9 due Dec '06.

- Spread of Shareholding ~ 2000 proxies issued for this Annual Meeting

- Cash retained at end of Sept ‘04 US$23.8 million
- Quarterly cash burn to end of Sept ’04 US$2 million

Corporate advisors:

- Lawyers – Morgan Lewis & Bockius – NY
- FDA advisors – MLB – Washington DC
- Auditors – BDO – US and Australia
- Brokers and dealers to the stock issues –
  UK – KBC Peel Hunt - London
  US – Janney Montgommery Scott – Philadelphia
- Investor relations – O'Connor – Sydney
- Public relations – Sciwords – Washington DC

2004 Announcements :

- Jan 23 -- Interview on MEI progress
- Feb 9 – Yale study partial results
- Feb 22 – Cervical cancer trial commencement
- Mar 8 – Renal cancer trial commencement
- Mar 26 – Four abstracts at ACCR meeting
- Mar 31 – Abstracts presented
- Apr 21 – New Yale ovarian cancer trial
- May 17 – MEI chairman honoured
- Jun 14 – New ovarian cancer trial site
- Nov 7 – FDA grants phenox “Fast Track” for ovarian cancer
- Nov 22 – Report on Oral phenox in prostate cancer

Committed phenoxodiol programs:

- Ovarian study – Yale / Melbourne
- Prostate study – Melbourne / Perth [complete]
- Cervical study – Yale
- Renal study – Sydney

Possible studies:

- Ovarian phase II/III – multi-center “fast track”
- Prostate phase II/III – multi-center
- Cervical ongoing
- Renal ongoing

Clinical management matters:

- drug availability
- drug cost
- patient recruitment rates = # of centers
- clinical management companies (CRO's)
- clinical management staff
- trial costs

Manufacturing and regulatory affairs:

- Scale up for oral and IV dose forms
- Therapeutic Goods Administration Licence (Aust) for capsules and sterile IV dose form manufacturing
- Out-sourcing R&D for – improved process engineering - and - chirality issues.

Out-licensing strategy for phenoxodiol:

- value proposition for phenox is increasing with trial success
- “Fast track” is vital sign that phenox is a player in oncology drug development
- data from trials will be published by clinicians as they deem appropriate
- from later in 2005, MEI may accept overtures for out-licensing discussions

In-licensing strategy:

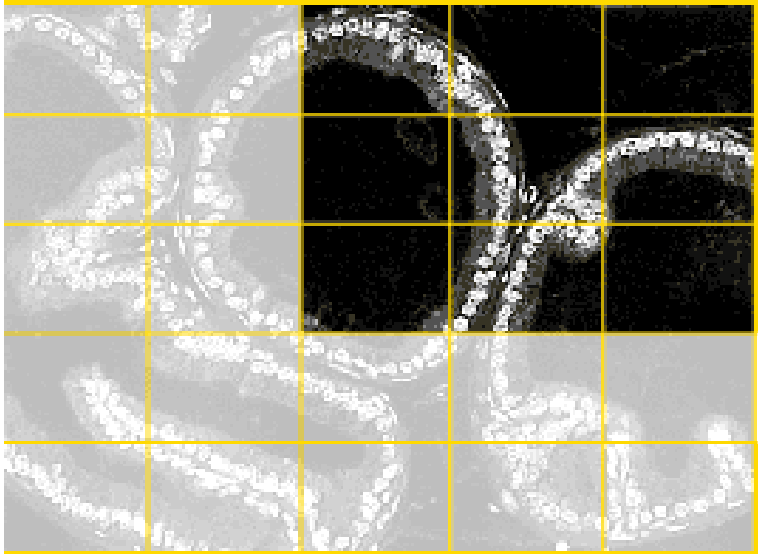
- MEI advised by Novogen that NV-18 is an "option compound", now in phase I
- MEI has commissioned a) patent report* b) independent confidential valuation of NV-18*
- MEI will wait for initial clinical insights*
- Novogen has advised that it has other potential oncology compounds in pre-clinical*
- MEI will assess these factors * before and during negotiation for further compound(s)

Future financing:

- Clinical expansion, multi-center trials
- New compound potential in-licence
- Virtual company more efficient
- Out-licensing is cash inflow
- Most appropriate time is after data is presented.

Company positioning:

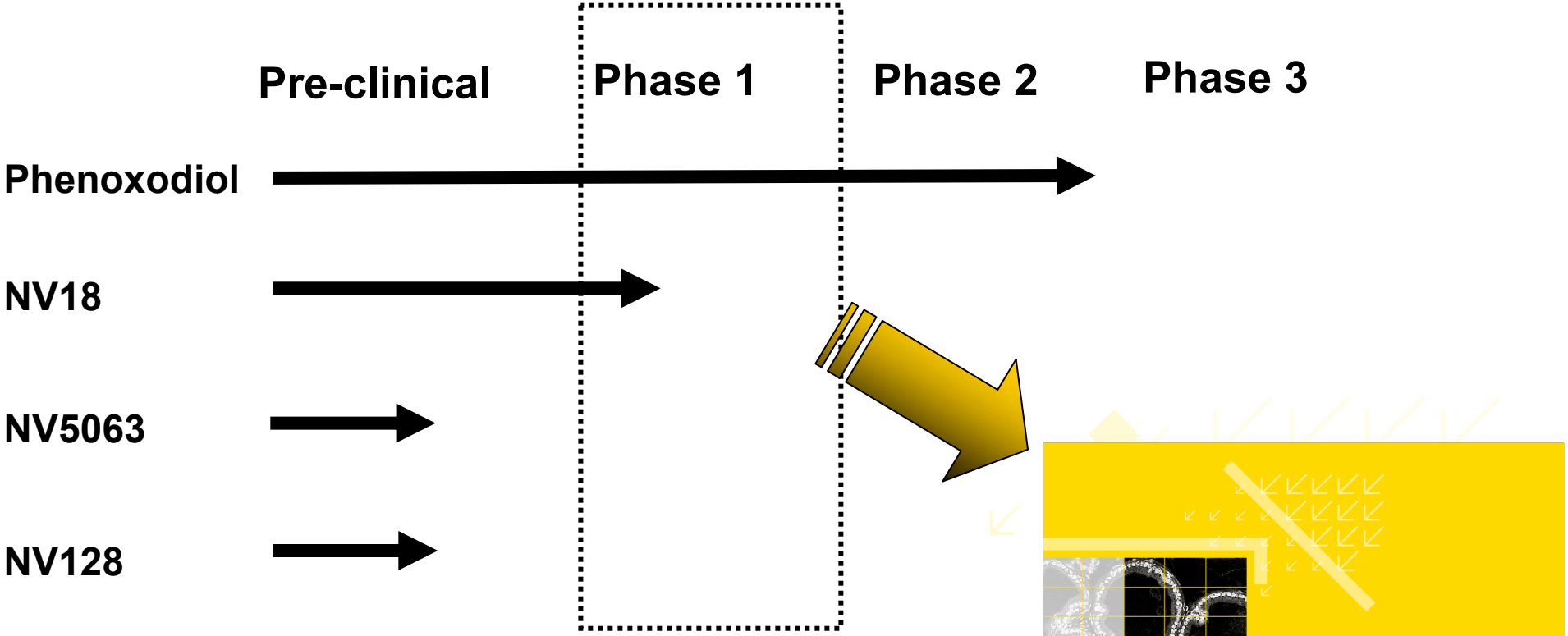
- Discovery X
- Development X
- Pre-clinical X
- Clinical MEI
- Registration possible MEI
- Marketing X
- Sales /Distribution X

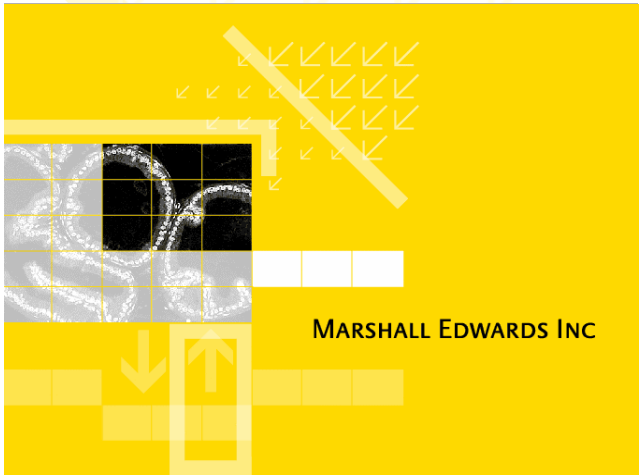


# Marshall Edwards Inc


## MARSHALL EDWARDS INC

- MEI has exclusive option over Novogen oncology drug pipeline.
- License opportunity activated by entry of drug into Phase 1 clinical trial.

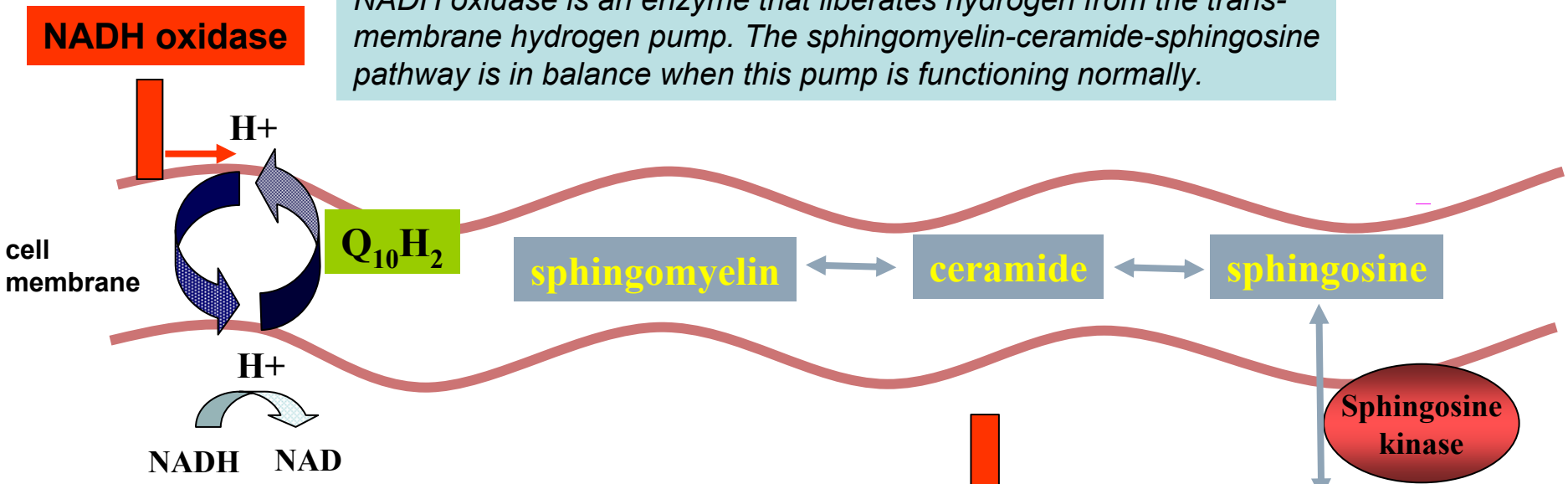


The anti-cancer drug pipeline has a number of unique features:

**(i) the target is a fundamental enzyme that regulates the 'survival-death' balance in cancer cells;**

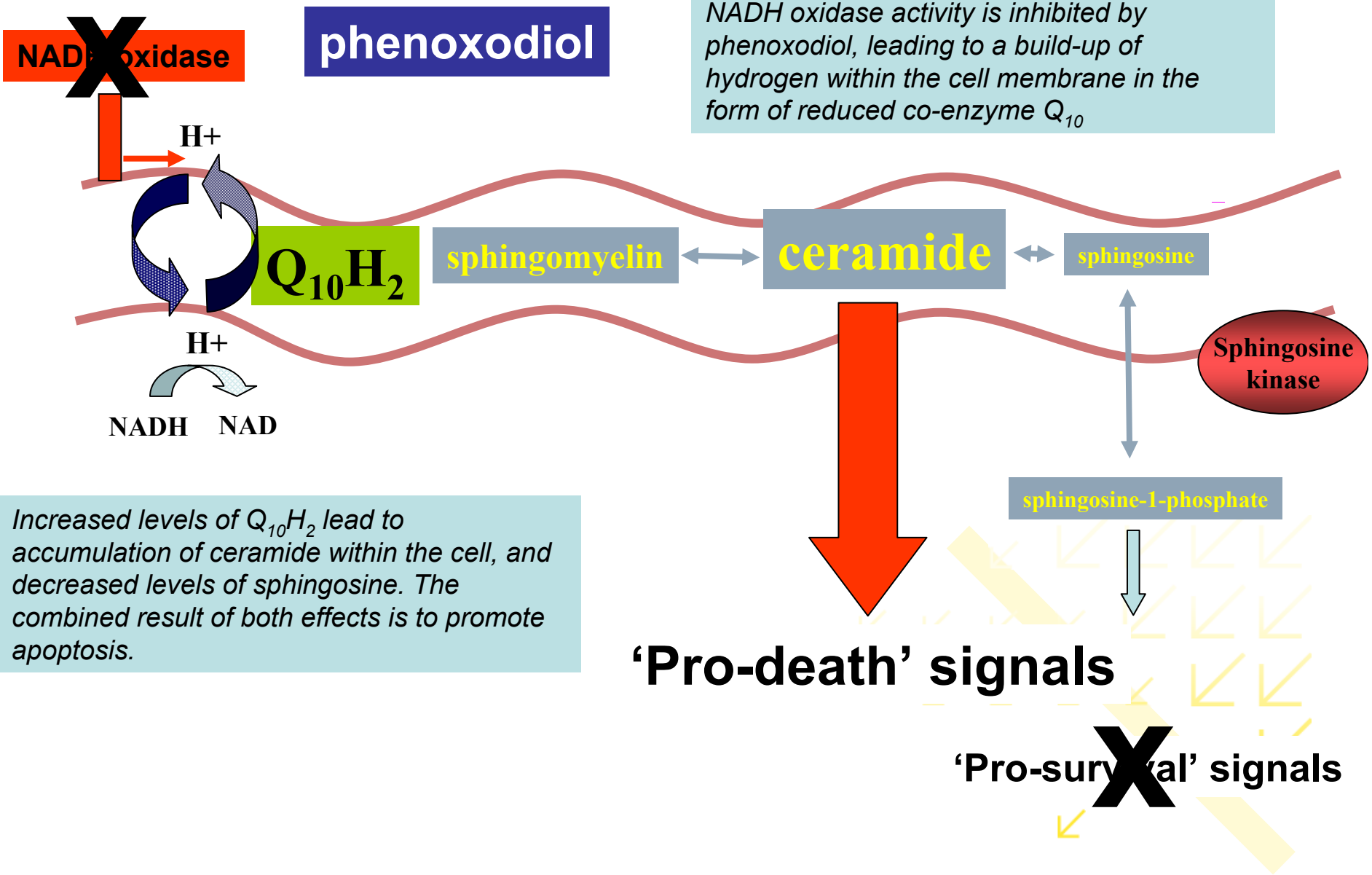
*NADH oxidase is an enzyme that liberates hydrogen from the trans-membrane hydrogen pump. The sphingomyelin-ceramide-sphingosine pathway is in balance when this pump is functioning normally.*




*Sphingomyelin forms the major part of the cell membrane. It is in a perpetual dynamic state, being converted sequentially to ceramide and then to sphingosine. Both ceramide and sphingosine are important secondary messengers within cells, with ceramide promoting cell death and sphingosine promoting cell survival.*

**'Pro-death' signals**

**'Pro-survival' signals**


NADH oxidase
phenoxodiol
NADH oxidase activity is inhibited by phenoxodiol, leading to a build-up of hydrogen within the cell membrane in the form of reduced co-enzyme $Q_{10}$
H+
$Q_{10}H_2$
sphingomyelin
ceramide
sphingosine
Sphingosine kinase
H+
NADH
NAD
sphingosine-1-phosphate
Increased levels of $Q_{10}H_2$ lead to accumulation of ceramide within the cell, and decreased levels of sphingosine. The combined result of both effects is to promote apoptosis.
'Pro-death' signals
'Pro-survival' signals

The anti-cancer drug pipeline has a number of unique features:

(i) the target is a fundamental enzyme that regulates the 'survival-death' balance in cancer cells;

**(ii) this target is confined to tumor cells, leading to high specificity and safety;**

**The NADH oxidase (NOX) that is present on all healthy cells is not affected by phenoxodiol.**

**The form of NADH oxidase that is present on human cancer cells is a different form, and is known as tumor-specific NOX, or tNOX. Phenoxodiol binds to this form, accounting for the high selectivity of phenoxodiol for tumor cells and the absence of toxicity in humans.**

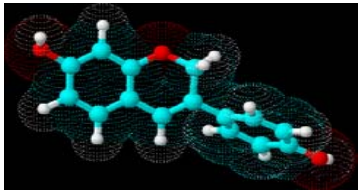
**The tNOX gene is present in adult stem cells and is thought to be an embryonic gene that is inactivated after birth, but reactivated with the development of cancer. Whether it is associated with the cause, or is the result of cancer developing, is under investigation.**

The anti-cancer drug pipeline has a number of unique features:

(i) the target is a fundamental enzyme that regulates 'survival-death' balance in cancer cells;

(ii) this target is confined to tumor cells, leading to high specificity and safety;

**(iii) minor structural changes to these compounds yields major changes in activity against different tumor cell types.**



# Phenoxodiol *(idronoxil)*

**Strategy # 1**

- late-stage cancers
- monotherapy or combinational therapy
- 'unmet clinical need'
- opportunity for accelerated approval based on surrogate indicators

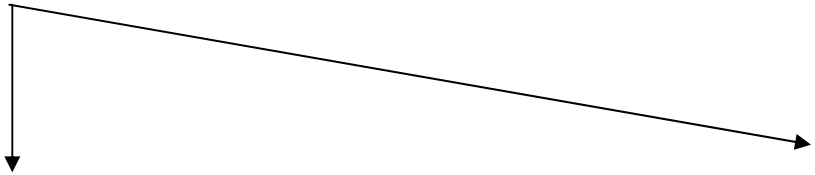
**Strategy # 2**

- early-stage cancers where early detection possible
- monotherapy
- longer trialling process, but significant opportunity

# FDA ONCOLOGY DRUG REVIEW

## ‘Unmet medical need’

The medical need is not addressed adequately by existing therapy.



**No existing therapy**

1. Not drugs used off-label
2. Not drugs with accelerated approval

**Inadequate existing therapy**

1. Significantly improved benefit
2. Broader effect on disease outcomes
3. Effective in unresponsive patients
4. Equivalence, but less toxic
5. Equivalence, but more practical

# Fast Track Program

Designed to facilitate the development and to expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet clinical needs.

Drugs in clinical use must demonstrate "an anti-tumor effect that confirms their potential to meet the unmet need"

# Fast Track Program

Benefits:

(i) facilitated meetings with FDA

(ii) submission of NDA in sections rather than simultaneously

(iii) increased likelihood of priority review

(iv) increased likelihood of accelerated approval

# Accelerated Approval

FDA may grant Accelerated Approval prior to completion of pivotal study on the basis of:

(i) effect on accepted surrogate end-points (eg. tumor markers) that 'are reasonably likely to predict clinical benefit'

(ii) effect on clinical end-points (eg. tumor size) other than survival that 'are indicative of clinical benefit'

(iii) post-marketing completion of pivotal study showing survival benefit and confirming predictive ability of (i) or (ii).

# Phenoxodiol – 'unmet clinical needs'

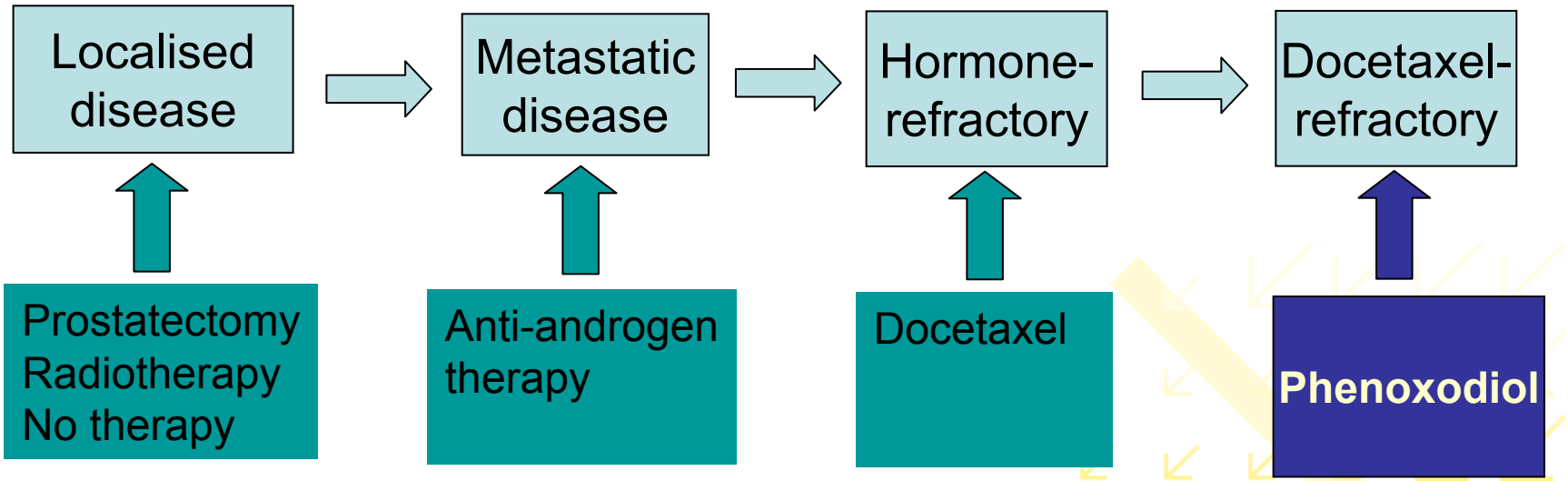
1. Hormone-refractory prostate cancer that has become unresponsive to docetaxel *(no approved therapies)*

2. Restoration of sensitivity to cisplatin in recurrent or persistent ovarian cancer that is cisplatin-refractory *(no approved therapies)*

3. Renal cancer that has become unresponsive to platinums *(no approved therapies)*

# Phenoxodiol

## Late-stage prostate cancer indication



# Phenoxodiol

## Prostate cancer indication **Phase Ib/IIa Study**

Subjects = metastatic HRPC
Rising PSA levels pre-study
Oral PXD monotherapy

| PXD Dose Stratum | n | PSA responses[1] | Patients with DP[2] by 6 months | Time to DP (weeks) |
|---|---|---|---|---|
| 20 mg | **6** | **0** | **6** | **9.6 (4-20)** |
| 80 mg | **6** | **0** | **6** | **9.0 (4-18)** |
| 200 mg | **5** | **1** | **2** | **n/a** |
| 400 mg | **4** | **2** | **1** | **n/a** |

1. > 50% fall in PSA levels compared to baseline
2. Disease progression

At low doses (20, 80 mg) of PXD:
- there was no PSA response
- all patients had DP by 6 months

At high doses (200, 400 mg) of PXD:
- 3/9 patients had a PSA response
- 6/9 patients had no DP by 6 months

- **steady-state plasma PXD levels**
- **no toxicity**

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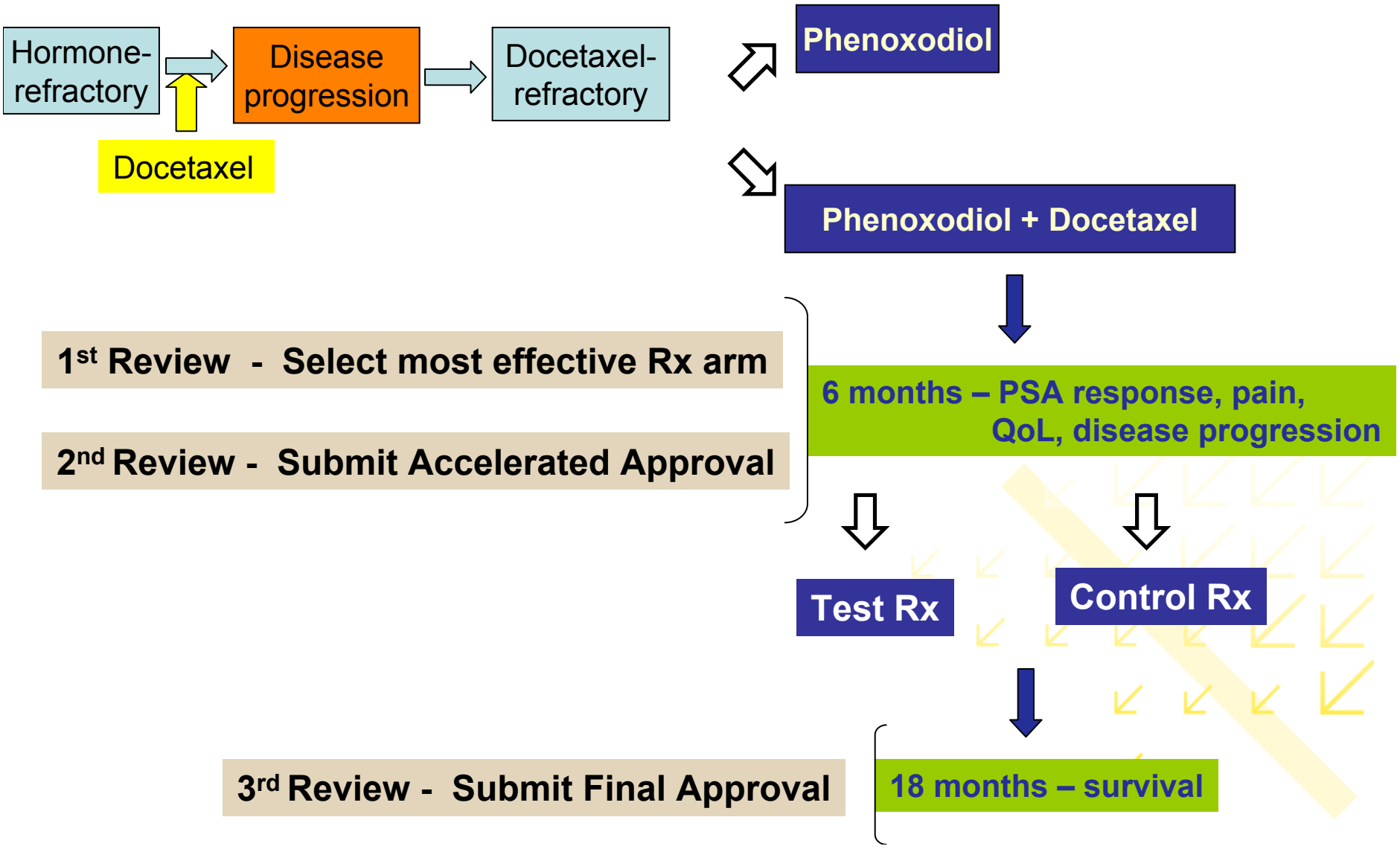
# Proposed Pivotal Study



# Phenoxodiol – 'unmet clinical needs'

1. Hormone-refractory prostate cancer that has become unresponsive to docetaxel *(no approved therapies)*

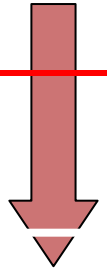
2. Restoration of sensitivity to cisplatin in recurrent or persistent ovarian cancer that is cisplatin-refractory *(no approved therapies)*

3. Renal cancer that has become unresponsive to platinums *(no approved therapies)*

# Phenoxodiol — Ovarian cancer indication program

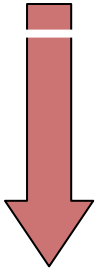
**Study NV06-0029**

**Recurrent ovarian cancer**
**PXD (intravenous) monotherapy**



**Study NV06-0037**

**Platinum- and/or taxane-resistant ovarian cancer**
**PXD (intravenous) + cisplatin or paclitaxel**



**Pivotal study**

**Cisplatin-refractory ovarian cancer**
**PXD + cisplatin**

**Study NV06-0024**

Results presented at SGO San Diego February, 2004 and AACR Orlando March 2004…:

At 6 wks: 6/40 patients responded (average 54% decrease CA125);
10/40 stabilized (CA125 levels stable)

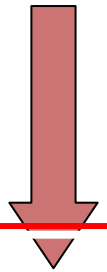
At 12 weeks, 10/40 patients remained stabilized

Following completion of the trial, 8/10 patients resistant or refractory to paclitaxel showed marked, declining levels of CA-125 on re-challenge with paclitaxel.

# Phenoxodiol — Ovarian cancer indication program

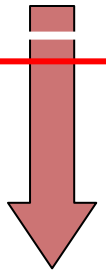
**Study NV06-0024**

**Recurrent ovarian cancer**
**PXD (intravenous) monotherapy**



**Study NV06-0035**

**Platinum- and/or taxane-resistant ovarian cancer**
**PXD (intravenous) + cisplatin or paclitaxel**



**Pivotal study**

**Cisplatin-refractory ovarian cancer**
**PXD + cisplatin**

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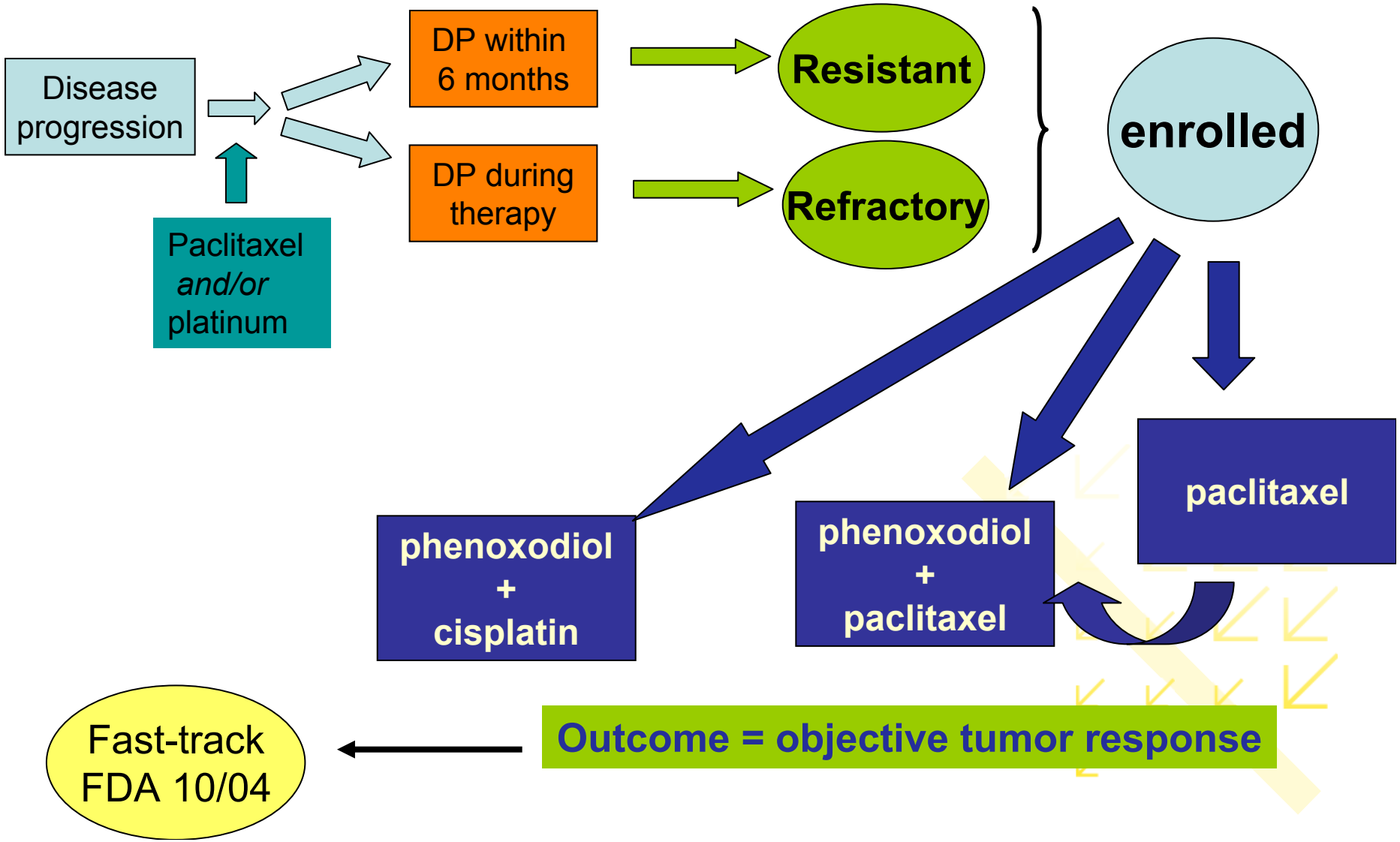
# Phenoxodiol

## Ovarian cancer indication

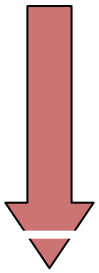
**Phase Ib/IIa Study**



# Phenoxodiol — Ovarian cancer indication program

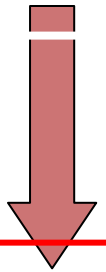
**Study NV06-0024**

**Recurrent ovarian cancer**
**PXD (intravenous) monotherapy**



**Study NV06-0035**

**Platinum- and/or taxane-resistant ovarian cancer**
**PXD (intravenous) + cisplatin or paclitaxel**



**Pivotal study**

**Cisplatin-refractory ovarian cancer**
**PXD + cisplatin**

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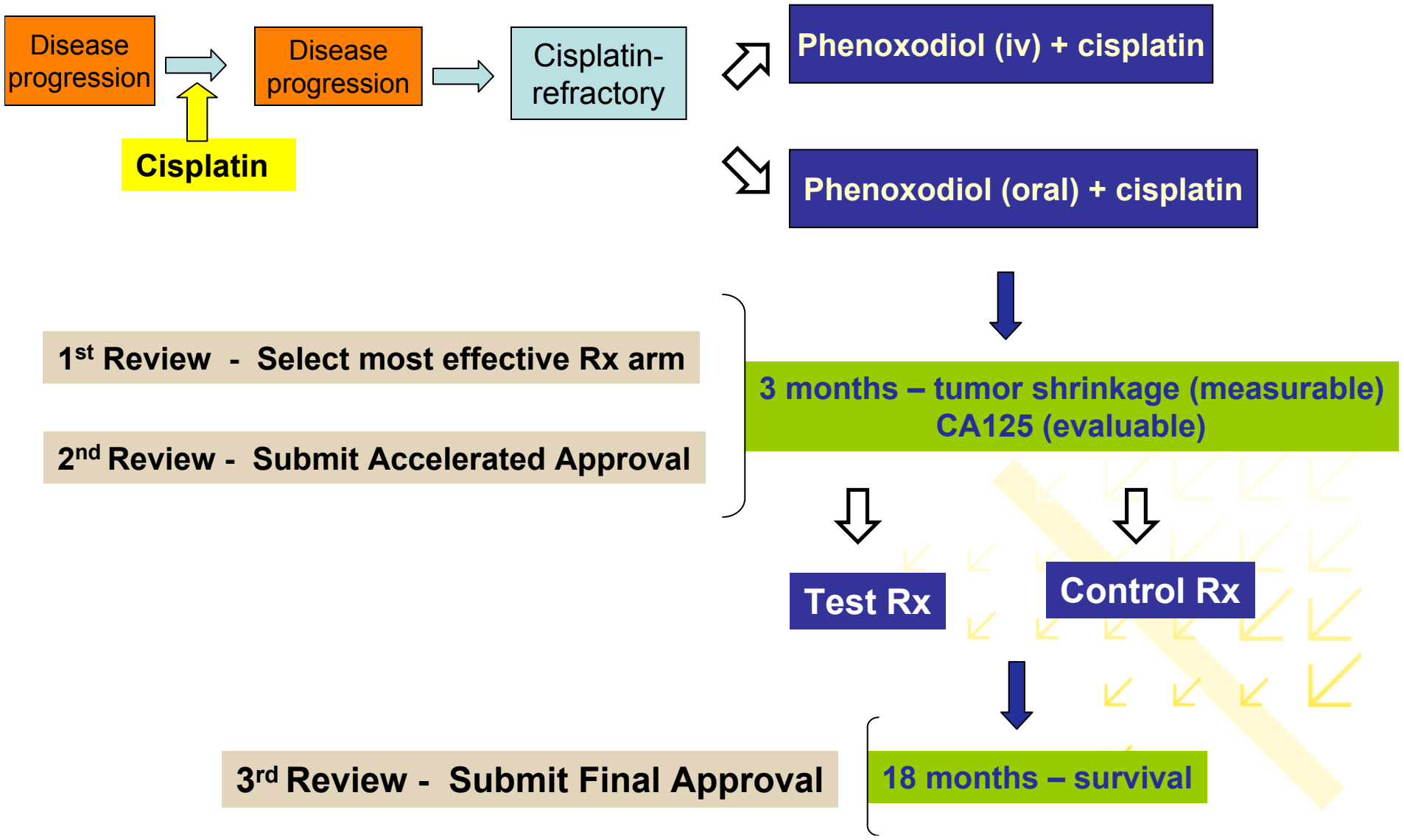
# Proposed Pivotal Study



## FDA ONCOLOGY DRUG REVIEW

# Phenoxodiol – *accelerated approval potential*

1. **Pivotal STUDY** (docetaxel-refractory HRPC) –
   *at 6 months:*
   - ⇨ PSA response
   - ⇨ pain level
   - ⇨ lack of disease progression (number of bone lesions, PSA levels)

2. **Pivotal STUDY** (platinum-refractory ovarian cancer)
   *at 3 months:*
   - ⇨ tumor shrinkage
   - ⇨ lack of disease progression (CA125 levels)

# Anti-cancer Pipeline Compound

**NV-18** : Targets: melanoma, pancreatic cancer, cholangiocarcinoma.

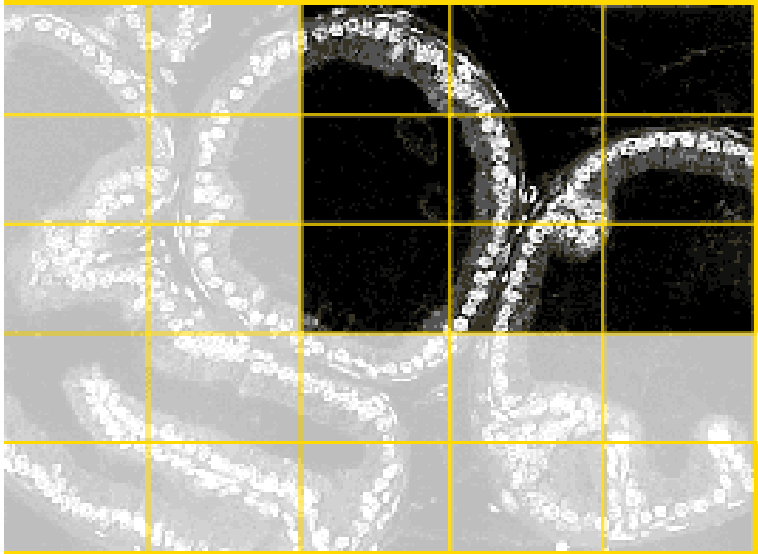
Chemo-sensitizer of cisplatin.

**Currrently in Phase Ia - Bio-availability, Pharmacokinetic and Acute Safety**

**NV-5063** : Target: hematological cancers.

Chemo-sensitizer of doxorubicin

**Currently completing pre-clinical safety studies**



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