

# **Drug Repurposing: looking ahead while checking the rear view mirror**

Numedicus (est. 2008) provides collaborative & consultative services to companies seeking expert advice in the area novel uses for existing drugs

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## Track Record

- Therapeutic areas

acute myocardial infarction  
cachexia  
diabetic retinopathy  
Dupuytren's contracture  
nausea and vomiting  
Raynaud's phenomenon  
retinal ischaemia  
depression  
Parkinson's disease

fibromyalgia  
functional bowel disease  
stress incontinence  
cancer fatigue  
glaucoma  
hypertrophic scarring  
leg ulcers  
neuropathic pain  
asthma  
diabetic nephropathy

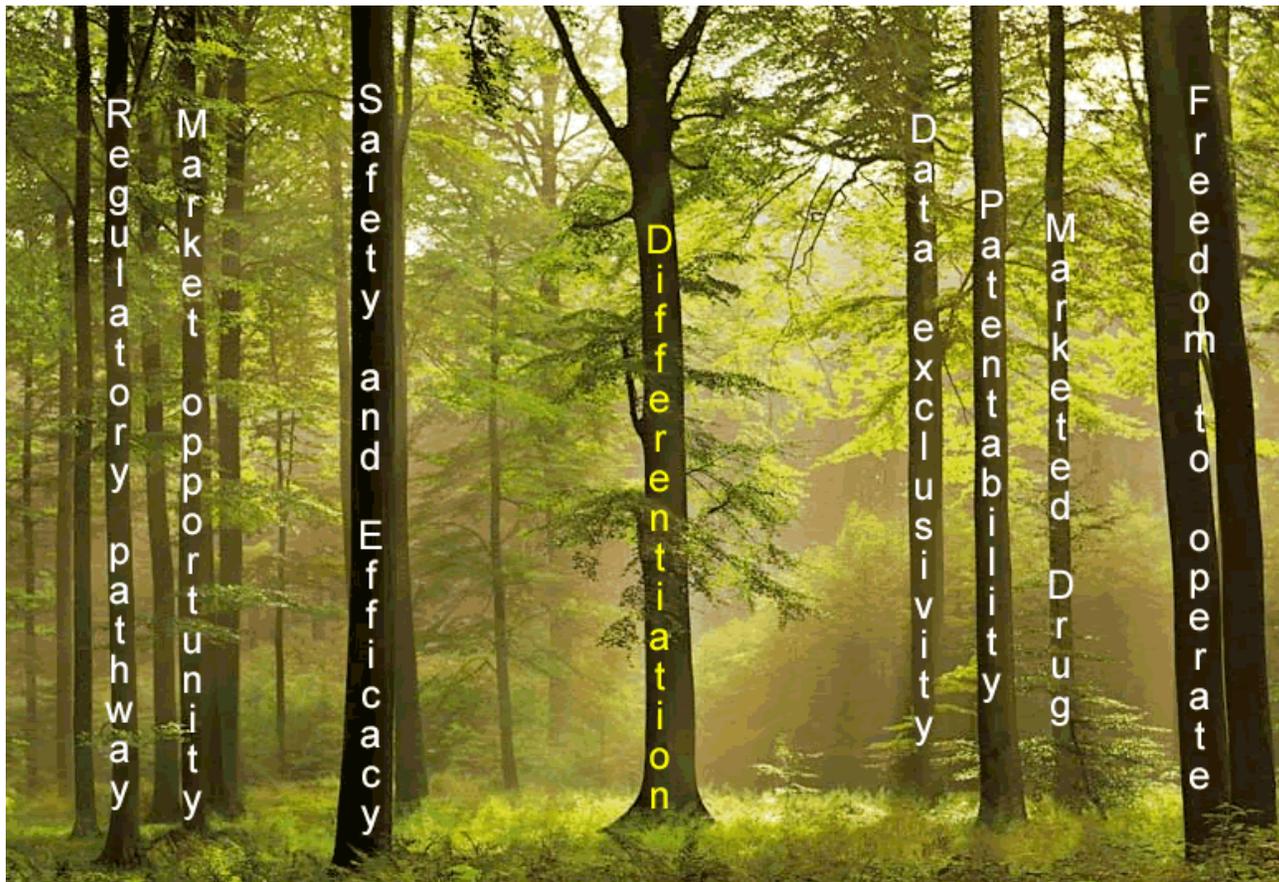
nociceptive pain  
overactive bladder  
premature ejaculation  
pulmonary hypertension  
reperfusion injury  
restenosis  
rosacea  
scleroderma  
anxiety

- Two repurposing projects taken to Phase II
- Multiple method of use patents granted

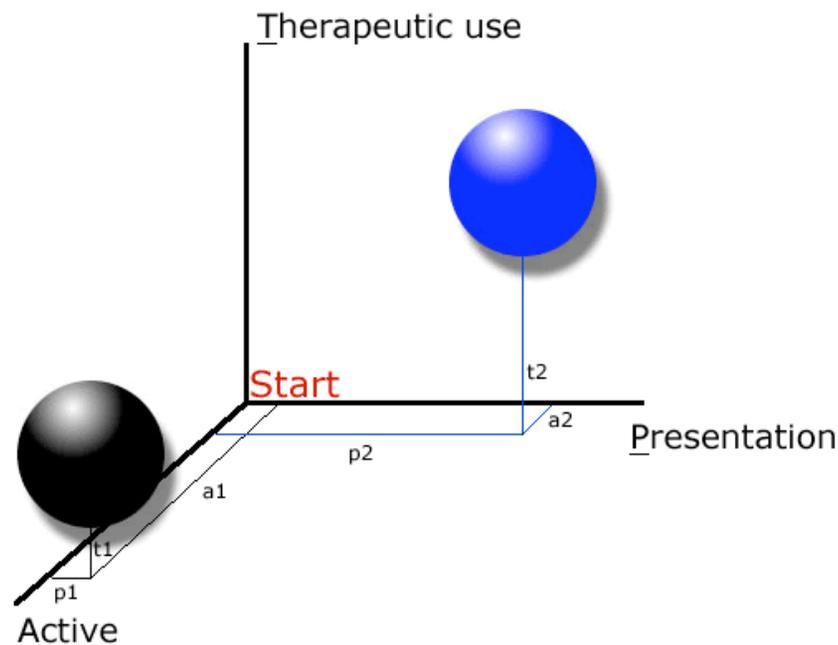
## Pinch points

- Plenty of new uses for existing drugs
- Opportunities limited by
  - *commercialisation issues*
  - patentability, freedom to operate issues
- Other issues
  - *quality of new data*
  - availability of old data
  - regulatory pathway

## Therapeutic Switches – Route finding



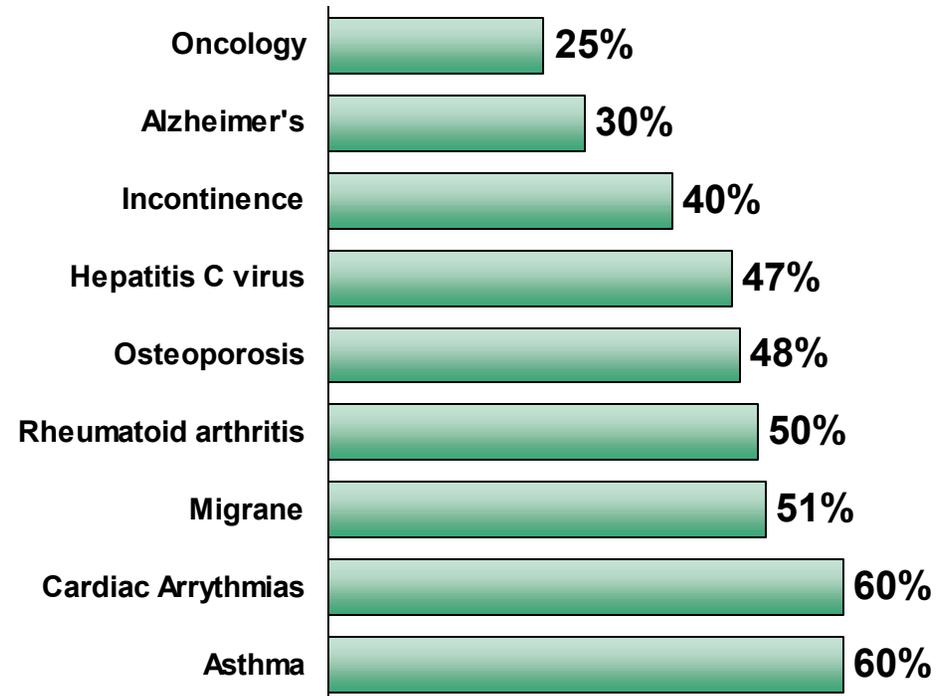
## Differentiated products -- APT



- Risk most correlated with distance from Active axis
- Differentiation correlated with sum of APT ordinates
- Low risk and high differentiation are possible (blue sphere)
- Is risk correlated with commercial value?

## Retrospective CT analysis

- Can provide excellent project validation
  - New indications
  - Patient sub-group
- Not the same as prospective trials
- Problem of confounds
- Limited by what has been or can be measured



Percent responders, by indication

## Retrospective CT examples 1

<b>Drug</b>	<b>Class of drug</b>	<b>New use</b>	<b>Basis for new use</b>
Aspirin	Cox inhibitor	Colorectal cancer	Rothwell PM et al, Lancet, 377, 9759, 31-41
Tamoxifen	Estrogen receptor modulator	Acute Coronary Syndrome (ACS)	Braithwaite et al, J. Gen. Intern. Med. 2003, 18(11), 937-47
Angiotensin II blockade	Angiotensin II antagonists	Hepatic fibrosis	Corey et al, Liver Int. 2009, 29(5), 748-53
Statins	HMG-CoA reductase inhibition	Epilepsy	Etminan et al, Neurology. 2010 75(17):1496-500

## Retrospective CTs – Cancer focus

Drug	Class of drug	New use	Basis for new use
Raloxifene	SERM	Breast cancer	Cummings et al JAMA 1999, 281, 2189-2197
Metformin	Insulin sensitizer	Breast cancer	Jiralerspong et al, J. Clin. Oncol. 2009, 27(20), 3297- 3302
Chlorimipramine (and others)	Tricyclic antidepressant	Cancer (glioma and colorectal cancer)	Walker et al, Br J Cancer , 2011, 104, 193 – 197

## Retrospective CTs – beta blocker focus

Drug	Class of drug	New use	Basis for new use
Propranolol	Beta-blocker	Osteoporosis	Wiens M et al, J Intern Med. 2006, 260(4):350-62
Propranolol	Beta-blocker	Melanoma	Di Georgi et al Arch Intern Med. 2011, 171(8),779-81
Propranolol/etodolac	Beta – blocker/NSAID <sup>1</sup>	Cachexia	Anker SD, et al. J. Am. Coll. Cardiol. 2003; 41 (Suppl. 1): 156A
MT-102 <sup>2</sup>	Catabolic-anabolic transforming agent		

<sup>1</sup> Combination being developed by Vicus.

<sup>2</sup> Being developed by PsiOxus, referred to as a ‘beta-blocker and catabolic/anabolic transforming agent’ in Scrip Intelligence 2010, 3528, 11.

## Conclusion

- Drug repurposing opportunities easy to identify, but often hampered by commercialisation issues
- Small API and formulation changes can be good bases for differentiated products
- Retrospective clinical trial/epidemiological evidence is a huge, relatively untapped source of new opportunities