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Disclaimer:

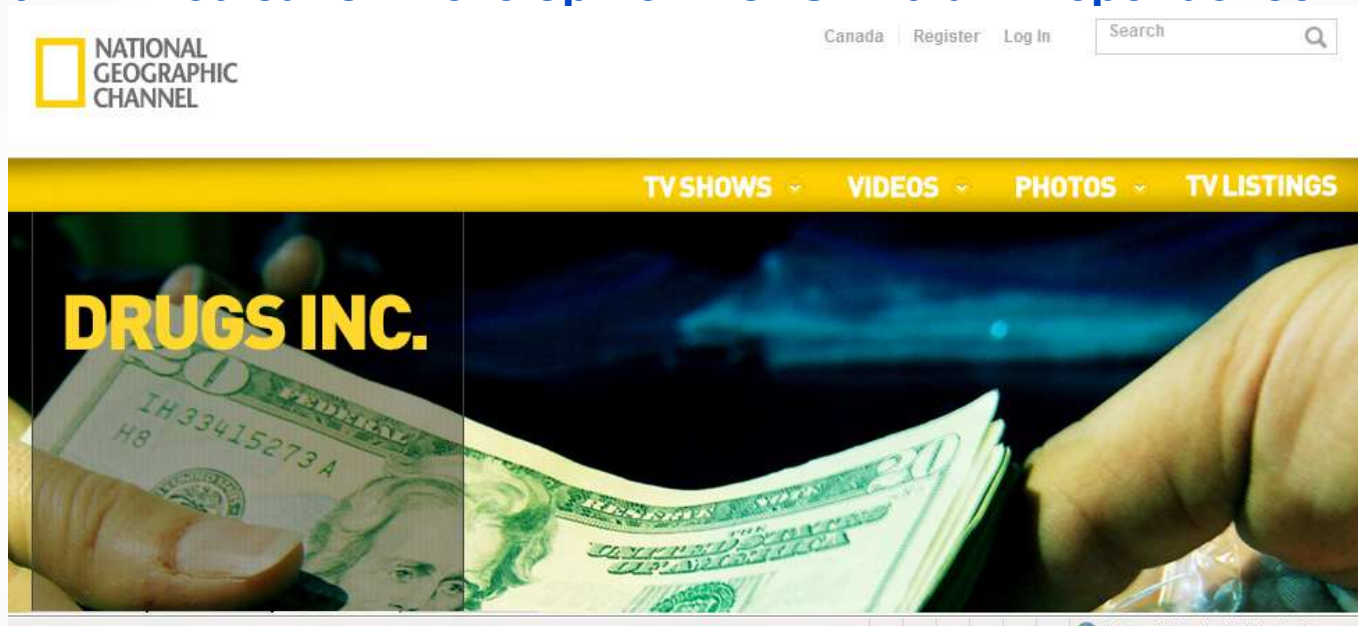
Dr. Palumbo is a full-time employee of the Mitsubishi  
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He is a member of the faculty at Yale University

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## 2012 Autumn: Medication Development for Stimulant Dependence Workshop



- **Stimulant use disorders**
  - Common
  - Animal models are compelling
  - Evidence of pharmacotherapeutic effects in humans
  - Cultural influences ubiquitous

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### Cocaine Farm

Meet a Colombian cocaine farmer, for whom growing any other crop would condemn him and his family to poverty.



### A Loco Habit

Traffickers smuggle cocaine across the border, into the hands of crack-cocaine addicts like 49 year old Loco.



### Addictive Imagery

Research suggests that cocaine is so addictive that simply showing images of its use can lead to a relapse.



### Cocaine Lab

A war against cocaine. Special forces prepare to destroy a cocaine laboratory in Columbia.



### Angels and Demons

A former addict talks about her road to addiction and the different drugs that lead her to methamphetamine. (02:59)



### Meth Brain

A neuropsychiatrist investigates how drugs work and specifically how methamphetamine affects the brain. (02:59)



### Crystal Clubbing

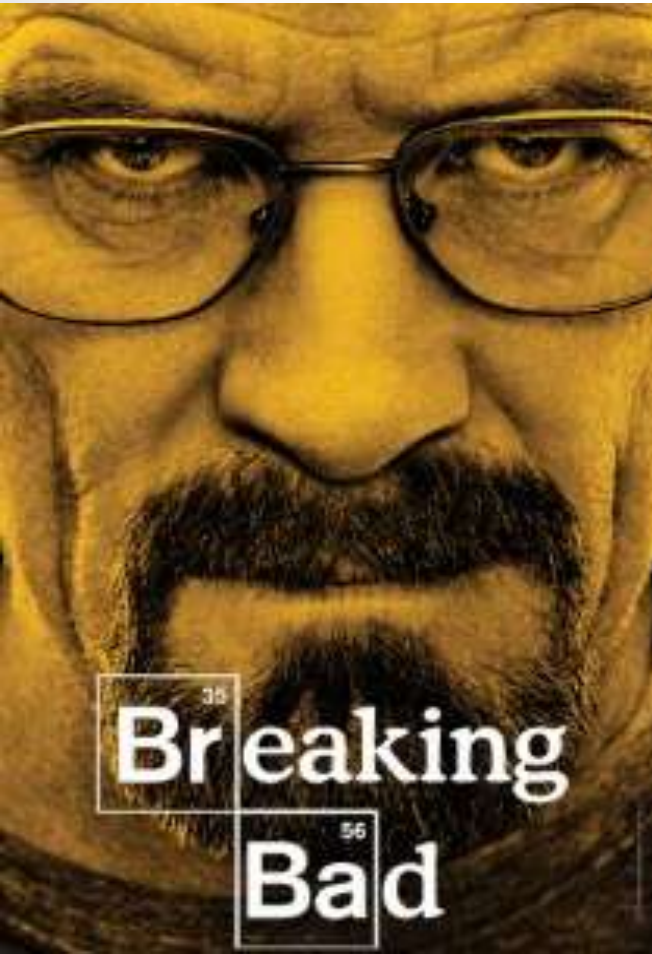
Discover the effects methamphetamine has had on San Francisco's Gay club scene; and the danger of unsafe sex. (02:59)



### Chronic

Raised on plastic spoons and dope by his gang-banging brother, 28 years old Chronic was born to be a crack dealer. (02:59)

## Despite the Fascination, Where are the Pharmacologies?



<sup>35</sup>  
**Breaking**  
<sup>56</sup>  
**Bad**

### Addicted in Hollywood: Stars' Problems With Cocaine 'Still Going Strong'

By *Hollie McKay* / *Pop Tarts* / *Published July 29, 2011* / *FoxNews.com*



Charlie Sheen and Brooke Mueller before their 2009 split.

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### The Business Model:

- Prioritization is based on the ability to achieve a risk adjusted return on investment
- Executives (not all of whom are scientists or researchers) tend to believe that they understand risk in therapeutic areas and indications with which they have familiarity
- Reliance on “analogue” and “recent past experience” encourages engaging “the Devil you know, versus the Devil you don’t”
- This may lead, perhaps, to a tendency for industry leaders to severely underestimate risk in areas of past academic leadership or past perceived corporate strength, while overestimating risk in indications with which they are less expert or less familiar
- Bold rolls of the dice occur in the context of “high risk – high reward” if there is the perception that unique or special competence can modify risk

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### Estimating the Probability of Success:

- How likely is it that the drug will have a relevant clinical effect?
- How can we measure that effect?
- If we are successful in showing an effect, does it occur in an area that anyone cares about?
- If it does, will health authorities agree that the magnitude and duration of effect are good enough?
- How safe does the intervention need to be?
- Where are the potential prescribers?
- If the prescribers find value in the intervention, will the patients/ clients, care providers, and family members want this medication?
- And, if they do, who is going to pay for the drug?
- Is there a community that will advocate?
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## The Challenges:

- John Belushi is dead – there is a perception that cocaine is no longer a problem, and there seems to be no willing or attractive “role model” or “poster child” advocating for medical pharmacologic care
- Amphetamine users are perceived as either marginalized or as folk-heros; neither image is attractive for funding
- Stimulant users, their environment, their ability to cooperate and to be compliant with the “must haves” or regulated pharmaceutical research, and the nature of the individuals who provide their care are either unknown by, or frankly frightening to corporate research
- Investing in study design and protocol development and funding, in the absence of knowing “how to win” in the regulatory environment can be a “brick wall”, especially if development in another therapeutic indication is “cut and dry” in terms of predictive success, and/or charismatic advocacy by leadership to invest elsewhere
- The care community is diverse, diffuse, perhaps, lacking unity, and possibly hostile to medical pharmaceutical intervention
- Lack of prior commercial success, or clinical effects of large magnitude about which one might “rally around” remain chilling
- An absence of clarity regarding the probabilities of achieving technical, regulatory, or commercial success leaves all variables as unknowns, making predictions for investment especially vexing

## **2012 Autumn: Medication Development for Stimulant Dependence Workshop**

### The Solutions:

This ISCTM Working Group, the sessions, and larger plenaries that will follow, will provide in an open and transparent process, a vehicle by which government, regulatory agencies, academia, industry, and perhaps providers will be able to provide clarity, vision, and direction to the development of pharmacologic therapies for stimulant addiction.

We will publish our findings, and will serve the larger CNS community as a reference point on stimulant addiction and pharmaceutical development



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The methods by which we will seek to reduce risk for clinical development:

- We will reduce risk by documenting with certainty the medical need and demography of this population
- We will reduce risk in establishing a path by which meaningful improvement can be measured and maintained, in conjunction with each of the member stakeholders, thus creating a greater consensus towards regulatory clarity
- We will reduce risk through discussion of clinical and methodological strategies in a pre-competitive environment
- We will reduce risk through elucidation of the predictive pre-clinical and translational models in stimulant addiction to stakeholder members
- We will reduce risk by showing that the effects of stimulant use disorders are central to primary care in both current and possible future health care models
- Will be reduce risk by providing evidence to document that investment in clinical therapies for stimulant addiction may be transformational towards future success in CNS research
- We will reduce risk by demonstrating to stakeholders that there can be useful and helpful clarity in defining technical, regulatory, and commercial paths to success.