# biosciences MONOGCAM

The Mark of Individualized Medicine

Overview of *PhenoSense* Novel Drug Testing and *PhenoScreen* 

# **Overview of Preclinical Drug Development**



Tertiary Screening: PhenoSense<sup>™</sup> Novel Drug Testing (1-10 compounds)

# **Resistance Profiling for Novel HIV Drugs**

### PhenoSense™ HIV Novel Drug Testing

- "Gold Standard" full drug characterization
- Extensive characterization of lead-compounds
- Customized virus panels (5-200+ viruses)
- Set-up and QC for new drugs required
- PR/RT, integrase, and entry inhibitors

### PhenoScreen<sup>™</sup> HIV Novel Drug Screening

- Rapid testing of 10+ of compounds
- Standard virus panels and stocks\* (from 5 to 20 viruses)
- Reduced drug set up work = lower cost
- Shorter TAT
- Available for entry and RT inhibitors



# *PhenoScreen*<sup>™</sup>: Higher Throughput Novel Drug Screening

### Developed in response to customer demand: "Secondary screening"

- Historically, many companies performed MT-4 or PBMC-based assays = Costly (people, time, lab space, data quality)
- Pharma recognizes the advantages of PhenoSense technology in drug screening (standard PhenoSense currently utilized for lead compound identification with smaller numbers of compounds)
- Phenotypic data is needed to make early Go and No-Go decisions on compounds
- Outsourcing this work to Monogram may be more cost-effective than keeping it in-house.



# *PhenoScreen*™: Higher Throughput Novel Drug Screening

#### PhenoScreen Setup:

- One marketed drug is included in drug panel as "control".
- Drug potency against a panel comprised of drug sensitive virus (NL4-3) plus a set panel of 5 – 20 library viruses (cannot change throughout contract)
- Approximate IC50 values
- Approximate Fold changes relative to reference
- Access to Monogram scientists for data interpretation (and Eric)
- Summary report with Monogram's interpretation (for add'l. fee)



# *PhenoScreen*<sup>™</sup>: Higher Throughput Novel Drug Screening

#### **Client Commitments:**

- Minimum yearly commitment of 500 curves (serum: virus combinations @ \$100 per combination) = \$50,000 per year
- Minimum of 10 compounds per order (can include marketed drugs in same class to reach minimum)
- Compounds pre-weighed and dissolved in appropriate diluent at standardized concentrations
- Any available data on IC50, cytotoxicity, solubility, MW
- Any available data on special handling, carcinogenicity, etc.



# *PhenoScreen*<sup>™</sup>: Higher Throughput Novel Drug Screening

#### PhenoScreen results in:

- Higher throughput
  - Standard virus panels and stocks are used
  - More drugs and fewer viruses tested
  - Standard TAT = 14 days (7 day TAT possible for a premium)
  - Lead compounds can be identified, optimized prior to testing in PhenoSense Novel Drug testing assay ("Gold Standard")
- Quality data for the Pharma sponsor
- Monogram can offer at a lower price than Standard PhenoSense novel drug characterization





# PhenoScreen: Sample IC50 Data

monogram IC50 Summary Phengcreen											
Client:	PhenoScree	nClient				Project:	P98765				
Drug	Compound1	Compound2	Compound3	Compound4	Compound5	Marketeddrug					
Unit	(uM)	(uM)	(uM)	(uM)	(uM)	(uM)					
Toxicity (#											
dilns)	2	0	0	1	0	0					
Virus											
SensitveVirus	0.0003	0.0011	0.0027	0.0010	0.0005	0.0010					
ResistantVirus	0.0017	0.1530	0.7689	0.0373	0.0059	0.0158					
Virus1	0.0009	>10.0000	>10.0000	0.0559	3.7294	>0.5000					
Virus2	0.0098	5.1605	>10.0000	0.1545	1.3528	>0.5000					
Virus3	0.0125	>10.0000	>10.0000	1.6543	5.6081	>0.5000					
Virus4	0.0007	1.5295	5.4046	0.0543	0.0312	>0.5000					
Virus5	0.0059	>10.0000	>10.0000	0.2843	5.7959	0.3246					
Virus6	0.0014	0.0581	0.0533	0.0140	0.0002	>0.5000					
Virus7	0.0002	0.7678	1.7715	0.0148	0.0493	>0.5000					
Virus8	0.0005	0.1307	0.1920	0.0078	0.0012	0.1556					
Virus9	0.0002	0.1297	0.3110	0.0111	0.0027	0.2302					
Virus10	0.0003	1.2046	2.0627	0.0264	0.0071	0.1442					
Virus11	0.0003	0.0884	0.3022	0.0080	0.0033	0.1171					
Virus12	0.0002	0.0172	0.0584	0.0039	0.0006	0.0388					
Virus13	0.0534	0.2657	0.4441	0.4755	0.1526	0.0206					
Virus14	0.0032	>10.0000	>10.0000	0.3757	5.6535	0.0157					
Virus15	0.0002	0.3838	0.9173	0.0043	0.0283	0.0062					
Virus16	0.0014	0.0228	0.0710	0.0109	0.0077	0.0019					
Virus17	0.0032	2.5111	>10.0000	0.0735	0.3552	0.0078					
Virus18	0.0001	0.0594	0.4628	0.0075	0.0009	0.0027					
Virus19	0.0014	6.3646	>10.0000	0.3002	0.1417	>0.5000					
Virus20	0.0855	>10.0000	>10.0000	1.8324	>10.0000	>0.5000					

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# **PhenoScreen:** Sample Fold Change Data

			Fold Cha	Pheng <sub>creen</sub>				
Drug Unit	Compound1 FC(CNDO)	Compound2 FC(CNDO)	Compound3 FC(CNDO)	Compound4 FC(CNDO)	Compound5 FC(CNDO)	Marketeddrug FC(CNDO)	Marketeddrug FC(CNDO)	Marketeddrug FC(CNDO)
Toxicity (# dilns)	2	0	0	1	0	0	0	0
Virus								
SensitveVirus	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
ResistantVirus	5.67	139.09	284.78	37.30	11.80	15.80	15.80	49.89
Virus1	3.00	max	max	55.90	7458.80	max	max	max
Virus2	32.67	4691.36	max	154.50	2705.60	max	max	max
Virus3	41.67	max	max	1654.30	11216.20	max	max	max
Virus4	2.33	1390.45	2001.70	54.30	62.40	max	max	max
Virus5	19.67	max	max	284.30	11591.80	324.60	324.80	max
Virus6	4.67	52.82	19.74	14.00	0.40	max	max	max
Virus7	0.67	698.00	656.11	14.80	98.60	max	max	max
Virus8	1.67	118.82	71.11	7.80	2.40	155.60	155.60	320.94
Virus9	0.67	117.91	115.19	11.10	5.40	230.20	230.20	max
Virus10	1.00	1095.09	763.96	26.40	14.20	144.20	144.20	max
Virus11	1.00	80.36	111.93	8.00	6.60	117.10	117.10	max
Virus12	0.67	15.64	21.63	3.90	1.20	38.80	38.80	228.05
Virus13	178.00	241.55	164.48	475.50	305.20	20.60	20.70	max
Virus14	10.67	max	max	375.70	11307.00	15.70	15.80	max
Virus15	0.67	348.91	339.74	4.30	56.60	6.20	6.20	279.72
Virus16	4.67	20.73	26.30	10.90	15.40	1.90	1.90	122.02
Virus17	10.67	2282.82	max	73.50	710.40	7.80	7.80	max
Virus18	0.33	54.00	171.41	7.50	1.80	2.70	2.70	max
Virus19	4.67	5786.00	max	300.20	283.40	max	max	max
Virus20	285.00	max	max	1832.40	max	max	max	max

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