Venky Chakravarthy: Bio

Venky has been a SAS user since 1991. He has provided contract Statistical, PK/PD, Outcomes Research and Clinical Programming services in multiple therapeutic areas for the Life Sciences industry over the past 20 years. He has presented at local, regional, national and international SAS and industry specific forums. He is the author of numerous SAS papers. Venky graduated from Case Western Reserve University, Cleveland OH with a PhD in Social Welfare.

The Anatomy of Clinical Trials Data: A Beginner's Guide – Part 1

when there is reasonable evidence of an association of a serious hazard with the **drug**. It is basically a **warning** with a **black box** around it, hence the name.

MSUG: February 22, 2018

@Magnify Analytics

Presenter: Venky Chakravarthy
Contract SAS Clinical Trials Programmer

The Anatomy of Clinical Trials: A SAS® Programmer's pride

- Advances in medicine: have cured deadly diseases; stopped disease progression.
- As a SAS programmer/analyst, you can take great pride in contributing to this important human cause.

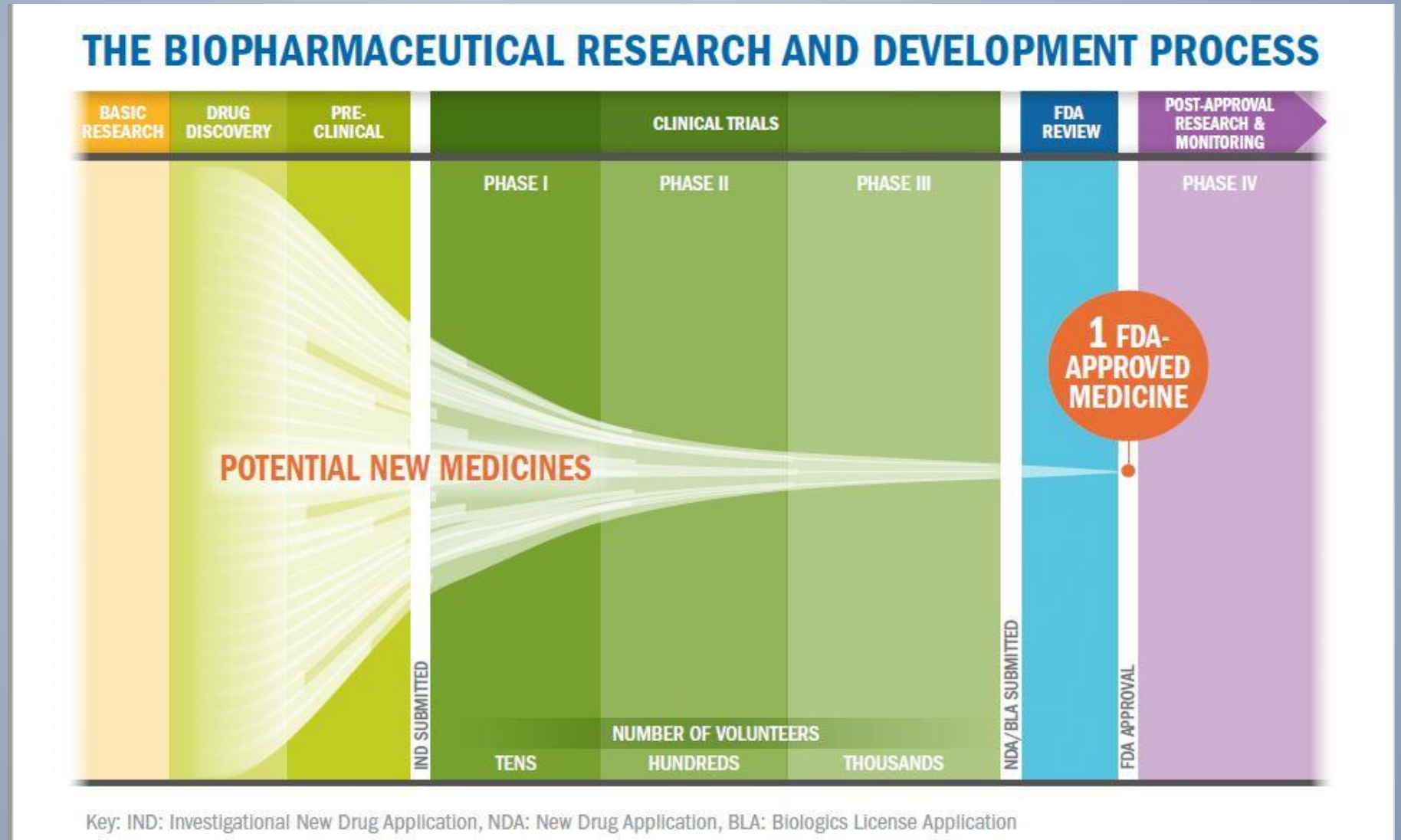
The Anatomy of Clinical Trials: Topic Layout

- Birth of a medicine – process involved.
- Length of time per stage – potential risks.
- Human trials (SAS programming)– likelihood of approval
- Human trials – Examples of 3 key ingredients
- A sample data collection plan – annotated

The Anatomy of Clinical Trials: Topic Layout

- Reign in wide disparities in data collection, interchange and reporting – STANDARDS
- Two key standards – (1) For Study Data Collection and Tabulation and (2) For Analysis and Reporting.

The Anatomy of Clinical Trials Data: Birth of a Medicine. Source: PhRMA



The Anatomy of Clinical Trials Data: Time by Each Stage. Source: Drug Discovery, 2004

	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PHASE III	OVERALL
Time per stage	3.5	0.46	1.4	2.3	5.1	12.9
Chance of failure	0.4	0.35	0.22	0.3	0.1	0.984
Progression probability	0.5	0.5	0.4	0.4	0.15	
Chance that one project entering this stage will eventually successfully leave it	0.58	0.52	0.42	0.52	0.44	
Number of projects needed to achieve one successful launch	30	13	6.2	3.6	1.7	

Drug Discovery World Fall 2004

The Anatomy of Clinical Trials Data: Likelihood of approval . Source: BIO Industry Analysis (2006-2015)

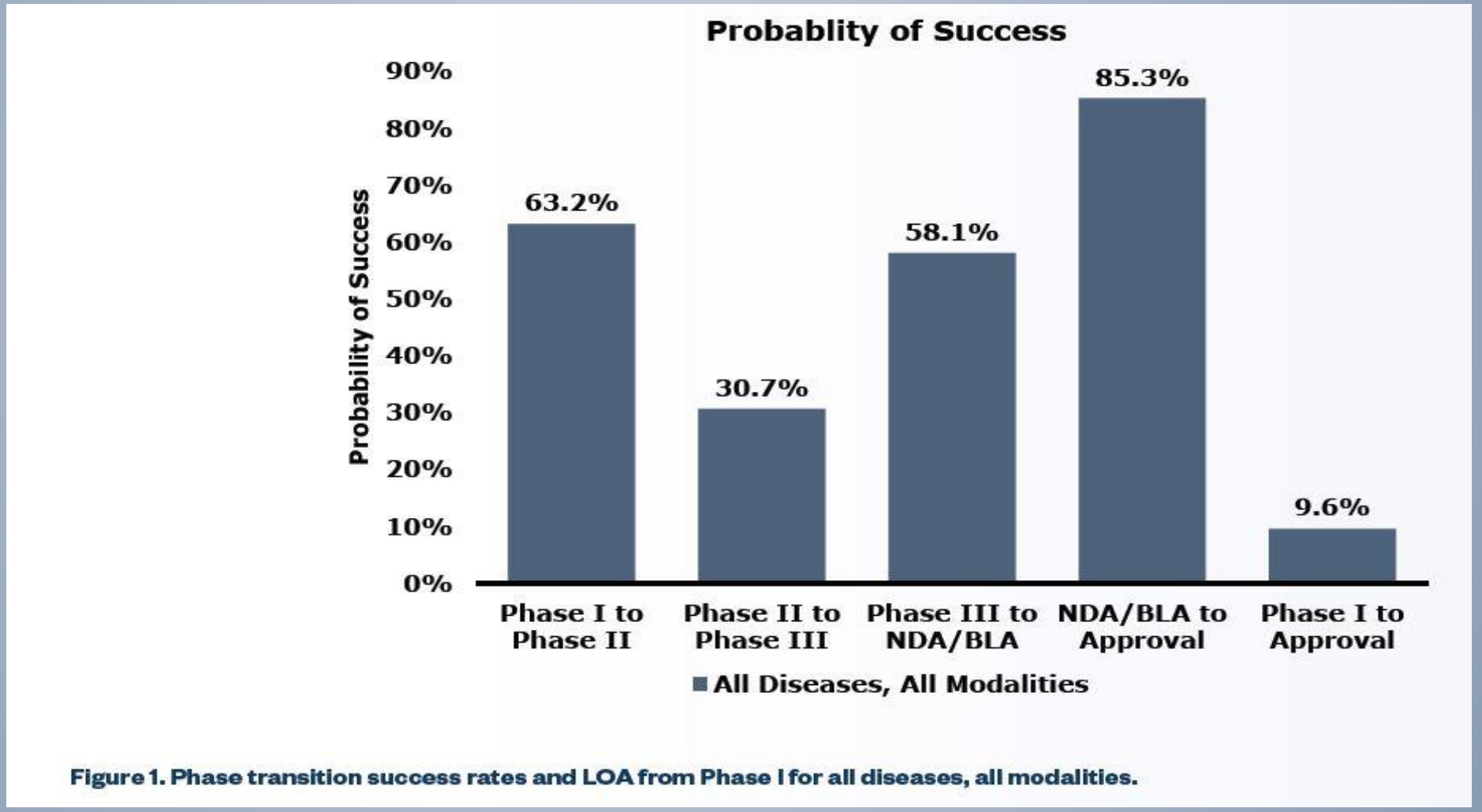


Figure 1. Phase transition success rates and LOA from Phase I for all diseases, all modalities.

The Anatomy of Clinical Trials: SAS Programming

- Trivia time
- Phases I-III (most common).
- Study plan: Protocol – Overall objectives of the study, what needs to be looked at to examine safety and efficacy of the drug. Involves multiple function areas involved in the conduct of a trial.
- Data collection plan : CRF - Detailed specifics for data collection : Example: Baseline information before the study drug is given. Demographics, Blood and Urine samples, Vital measures etc.
- Analysis and Reporting plan: SAP - Minute level specifications on what needs to be analyzed and the types of reports

The Anatomy of Clinical Trials: Data Standards, CDISC and FDA

› Electronic data capture: typically into Oracle Clinical with standard field names as Annotated in the CRFs. Raw data extracted to SAS. Source: Lee, K. SGF, Paper 396-2008

Screening

Protocol Study000	Site No. 000	Subject No. ☐☐☐☐	Subject Initials ☐☐☐

Informed Consent	
Date Informed Consent signed: (must be prior to all study procedures)	CONSDT ☐☐/☐☐☐/200☐ dd mmm yyyy
Time Informed Consent signed:	CONSTM ☐☐:☐☐ (24 hour clock)

Demographics			
Date of Birth: ☐☐ / ☐☐☐ / ☐☐☐☐ dd mmm yyyy BIRTHDT		Gender: SEX	☐Male (1) ☐Female (2)
Ethnicity (Check one box only):	RACE ☐ Caucasian (1) ☐ African American (2) ☐ Asian (3)	☐ Hispanic (4) ☐ Native American (5) ☐ Other (99) specify: _____ RACESP	

The Anatomy of Clinical Trials: Data Standards, CDISC and FDA

- CDISC emerged – volunteer organization from the industry to form standards for data collection, distribution and analysis. CDISC later became a non-profit and works closely with the FDA.
- Mission Statement: “The CDISC mission is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.”

The Anatomy of Clinical Trials: Data Standards, CDISC and FDA

- CDISC formulated two important models for clinical trials Study Data Tabulation Model (SDTM) and Analytical Data Model (ADaM).
- SDTM: Electronic listing of individual observations for each subject (in place of patient profiles). Has a standard data structure and standard variable names beginning with the domain name (AE, DM etc.) Names of lab tests and units are standardized (think like formats). A sample SDTM for EX follows.

The Anatomy of Clinical Trials: Data Standards, CDISC and FDA

› CDISC provides an implementation guide (SDTMIG) for companies to write specifications to construct SDTM. Here is a sample SDTM for Subjects' Exposure to the Study Drug. Domain is called EX.

STUDYID	DOMAIN	USUBJID	EXSEQ	EXGRPID	EXTRT	EXDOSE	EXDOSU	EXDOSFRM
56789	EX	56789001	1	1	DRUG A	20	MG	CAPSULE
56789	EX	56789001	2	1	DRUG A	20	MG	CAPSULE
56789	EX	56789001	3	1	DRUG A	20	MG	CAPSULE
56789	EX	56789001	4	2	DRUG B	30	MG	TABLET, COATED
56789	EX	56789001	5	2	DRUG B	30	MG	TABLET, COATED
56789	EX	56789001	6	2	DRUG B	30	MG	TABLET, COATED
56789	EX	56789003	1	1	DRUG B	30	MG	TABLET, COATED
56789	EX	56789003	2	1	DRUG B	30	MG	TABLET, COATED
56789	EX	56789003	3	1	DRUG B	30	MG	TABLET, COATED

The Anatomy of Clinical Trials Data: More Standards

- SDTM structure is fine but unsuitable to generate planned analysis.
- Enter Analytical Data Model (ADaM). Complex algorithms implemented to derive additional variables. Standard variable names added to facilitate analysis laid out in SAP (Quiz: recall what that is?). Limited to variables needed for analysis
- ADaM is also constructed based on an implementation guide (ADaMIG). Companies write ADaM specifications. Golden rule to be observed – must be able to reverse engineer to the source SDTM dataset(s).

The Anatomy of Clinical Trials Data: More Standards

- FDA mandates a subject level ADaM dataset (ADSL) to be submitted when seeking drug approval. Companies usually submit more than one ADaM. An implementation guide (ADaMIG) accompanies this standard. Golden rule – maintain traceability to the source SDTM dataset(s). A partial ADSL sample

Row	USUBJID	ARM	TRT01P	TRT01A	TR01SDT	TR01EDT
1	1001	Drug X 5 mg	Drug X 5 mg	Drug X 5 mg	23OCT2007	17DEC2007
2	1002	Placebo	Placebo	Placebo	19JUL2006	20SEP2007
3	1003	Drug X 5 mg	Drug X 5 mg	Placebo	01NOV2007	20NOV2007

The Anatomy of Clinical Trials: Conclusion

- Covered the birth process of a medicine.
- Covered the length of time and risks.
- Covered the 3 Phases of Human trials
- Covered the Key components in any Phase study – Study plan, Data collection plan and Reporting plan
- Covered the two main industry data standards for a SAS Programmer.

The Anatomy of Clinical Trials: Questions?

The Anatomy of Clinical Trials: Contact Information

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