Genomics at FDA: 2018 Year-in-Review

PGRN Meeting
December 7, 2018

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Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Medical Products and Biomarkers

Notable CY18 Approvals

Drug	Disease or Condition	Biomarker	Use
Patisiran*, Inotersen*	polyneuropathy of hereditary transthyretin-mediated amyloidosis	**N/A**	N/A
Tezacaftor* + ivacaftor	cystic fibrosis	**responsive CFTR variant**	Patient Selection
Migalastat*	Fabry disease	**amenable GLA variant**	Patient Selection
Ivosidenib*	relapsed or refractory AML	**susceptible IDH1 mutation**	Patient Selection
Binimetinib*, encorafenib*	metastatic melanoma	**BRAF V600E/K mutation**	Patient Selection
Dacomitinib*	metastatic NCSLC	**EGFR exon 19 deletion or L858R substitution**	Patient Selection
Larotrectinib*	solid tumors	**NTRK gene fusion**	Patient Selection
Gileritinib*	relapsed or refractory AML	**FLT3 mutation**	Patient Selection
Lorlatinib*	metastatic NCSLC	**ALK gene rearrangement**	Patient Selection
Talazoparib*	advanced or metastatic breast cancer	**Germline BRCA mutation**	Patient Selection
Afatinib	metastatic NCSLC	**Non-resistant EGFR mutation**	Patient Selection
Amifampridine*	Lambert-Eaton myasthenic syndrome	**NAT2 genotype**	Dosing
6-MP/TG	ALL/acute nonlymphocytic leukemia	**TPMT/NUDT15 genotype**	Dosing
Avatrombopag*	thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure	**FVL**	Warning
Lofexidene*	opioid withdrawal symptoms	**CYP2D6 genotype**	Informational
Elagolix*	severe pain associated with endometriosis	**SLCO1B1 genotype**	Informational

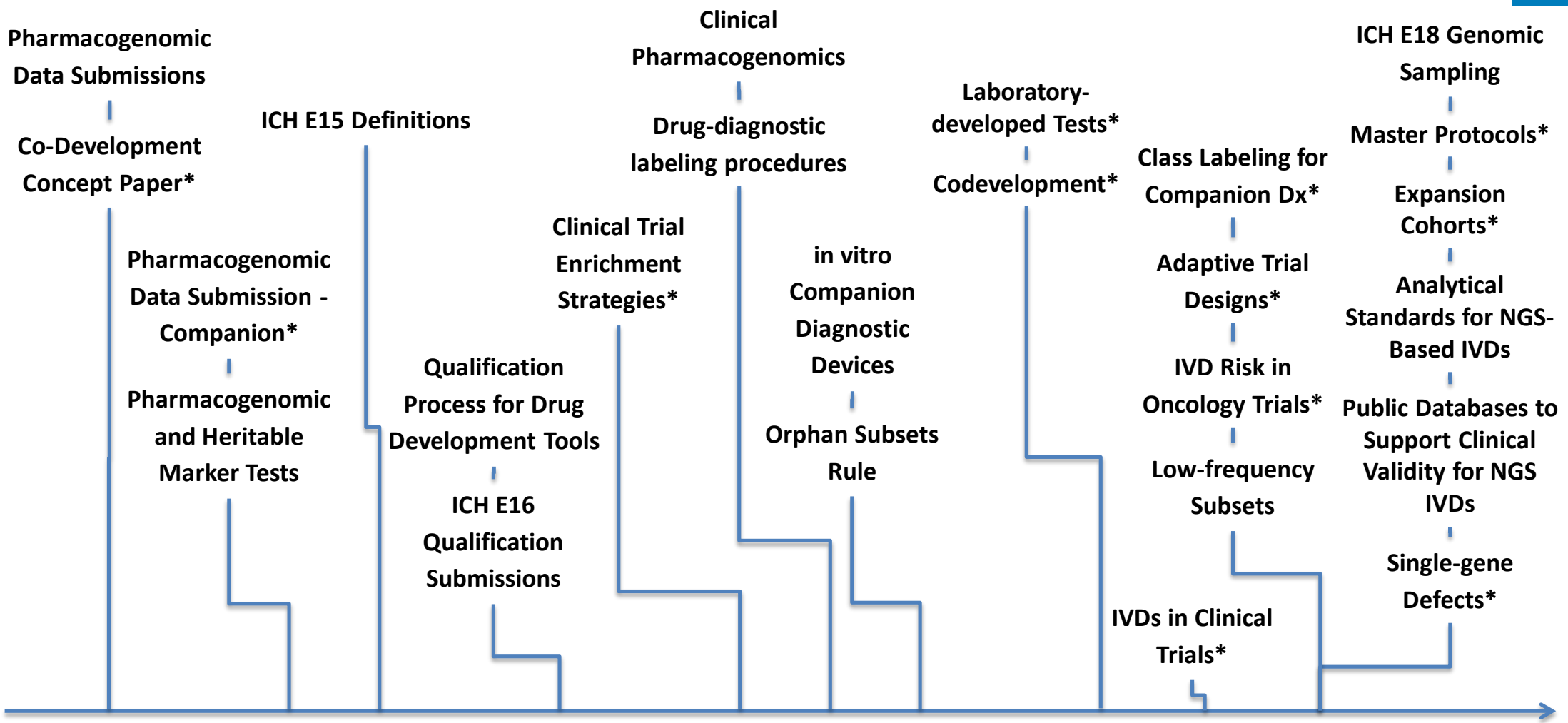
* New molecular entity

Medical Products and Biomarkers

- CDRH/in vitro diagnostic devices
  - 23andme Personal Genome Service Pharmacogenetic Reports authorized
  - ClinGen Expert Curated Human Variant Data recognized as source to support clinical validity

- Biomarker Qualification
  - Critical Path Institute/FNIH urinary nephrotoxicity biomarker panel (CLU, CysC, KIM-1, NAG, NGAL, OPN) to aid in detection of kidney tubular injury in phase 1 trials in healthy subjects

Guidance and Policy



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Research*

- Systems biology and genomic approaches to predict target-mediated adverse events
- Strengthening safety signals through population pharmacogenomics
- Utility of early-phase biomarker investigations in detecting significant safety issues
- Cost drivers for biomarkers in drug development
- Drug development practices
  - Clinical development of synthetic oligonucleotides
  - Dose-ranging and titration
  - Racial/ethnic composition of clinical trials

(CRADAs, contracts, grants, MOUs, RCAs, intramural)

* Reflects selected projects being led out of Genomics and Targeted Therapy Group in CDER's Office of Clinical Pharmacology; many additional research projects related to genomics and precision medicine across FDA

Outreach

- Public Workshop on Weighing the Evidence: Variant Classification and Interpretation in Precision Oncology
- FDA/OCE Public Meeting on Relevant Molecular Targets in Pediatric Cancers: Applicability to Therapeutic Investigation FDARA 2017
- Public Workshop on Tissue Agnostic Therapies: Regulatory Considerations for Orphan Drug Designation
- Public Meeting on Drug Development Tool Process under the 21st Century Cures Act and PDUFA VI (*upcoming – December 11, 2018*)

- PrecisionFDA challenges: https://precision.fda.gov/challenges

OCE: Oncology Center of Excellence