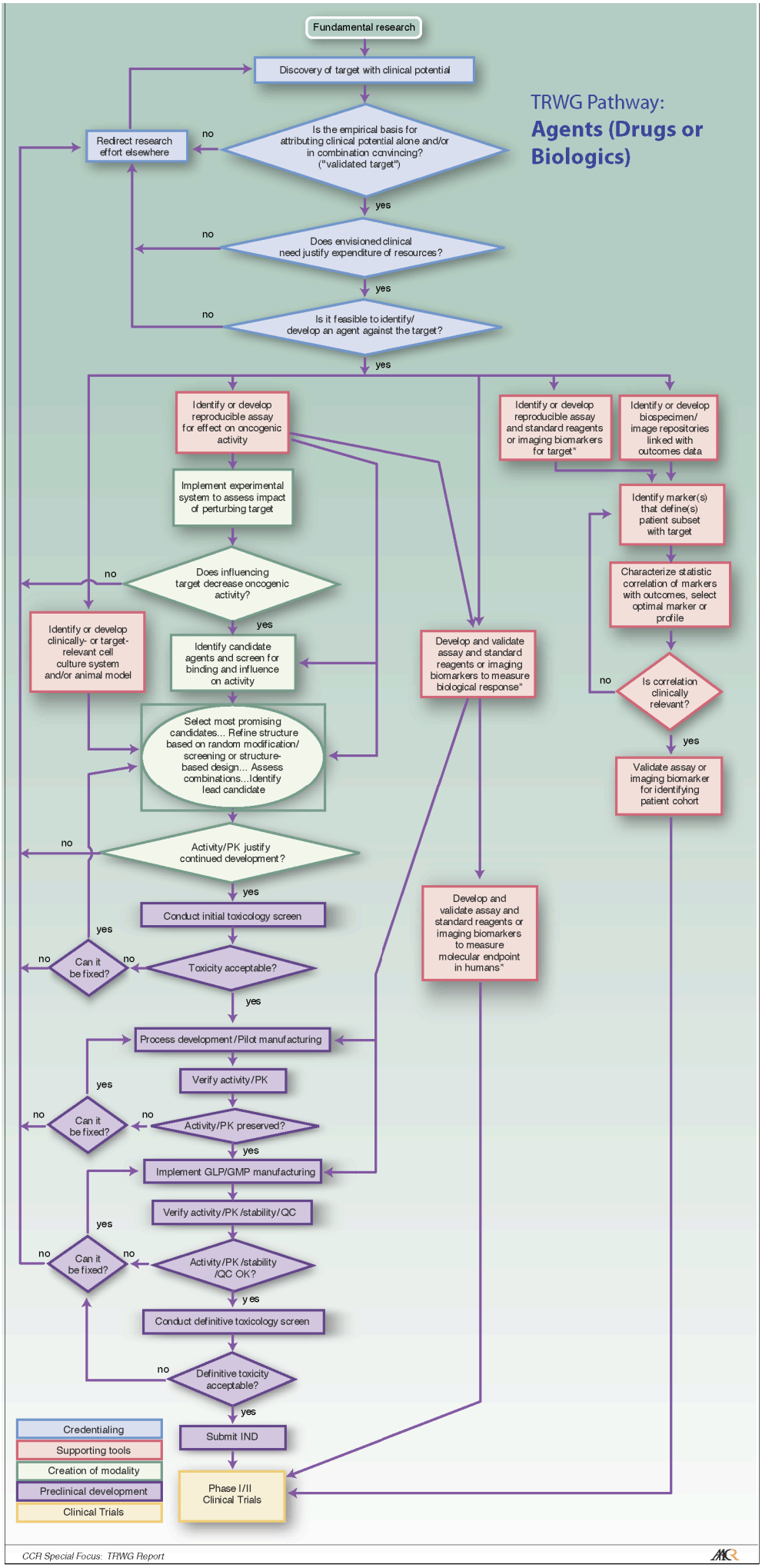
TRWG Pathway:
Agents (Drugs or Biologics)
Fundamental research
Discovery of target with clinical potential
Is the empirical basis for attributing clinical potential alone and/or in combination convincing? ("validated target")
Redirect research effort elsewhere
no
yes
Does envisioned clinical need justify expenditure of resources?
Is it feasible to identify/ develop an agent against the target?
Identify or develop reproducible assay for effect on oncogenic activity
Implement experimental system to assess impact of perturbing target
Does influencing target decrease oncogenic activity?
Identify or develop clinically- or target-relevant cell culture system and/or animal model
Identify candidate agents and screen for binding and influence on activity
Select most promising candidates... Refine structure based on random modification/ screening or structure-based design... Assess combinations...Identify lead candidate
Activity/PK justify continued development?
Conduct initial toxicology screen
Toxicity acceptable?
Can it be fixed?
Process development/Pilot manufacturing
Verify activity/PK
Activity/PK preserved?
Implement GLP/GMP manufacturing
Verify activity/PK/stability/QC
Activity/PK/stability /QC OK?
Conduct definitive toxicology screen
Definitive toxicity acceptable?
Submit IND
Phase I/II Clinical Trials
Identify or develop reproducible assay and standard reagents or imaging biomarkers for target*
Identify or develop biospecimen/ image repositories linked with outcomes data
Identify marker(s) that define(s) patient subset with target
Characterize statistic correlation of markers with outcomes, select optimal marker or profile
Is correlation clinically relevant?
Validate assay or imaging biomarker for identifying patient cohort
Develop and validate assay and standard reagents or imaging biomarkers to measure biological response*
Develop and validate assay and standard reagents or imaging biomarkers to measure molecular endpoint in humans*
Credentialing
Supporting tools
Creation of modality
Preclinical development
Clinical Trials