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Applied Translational Medicine

Effective Outsourcing of Clinical Pharmacology Studies in Europe

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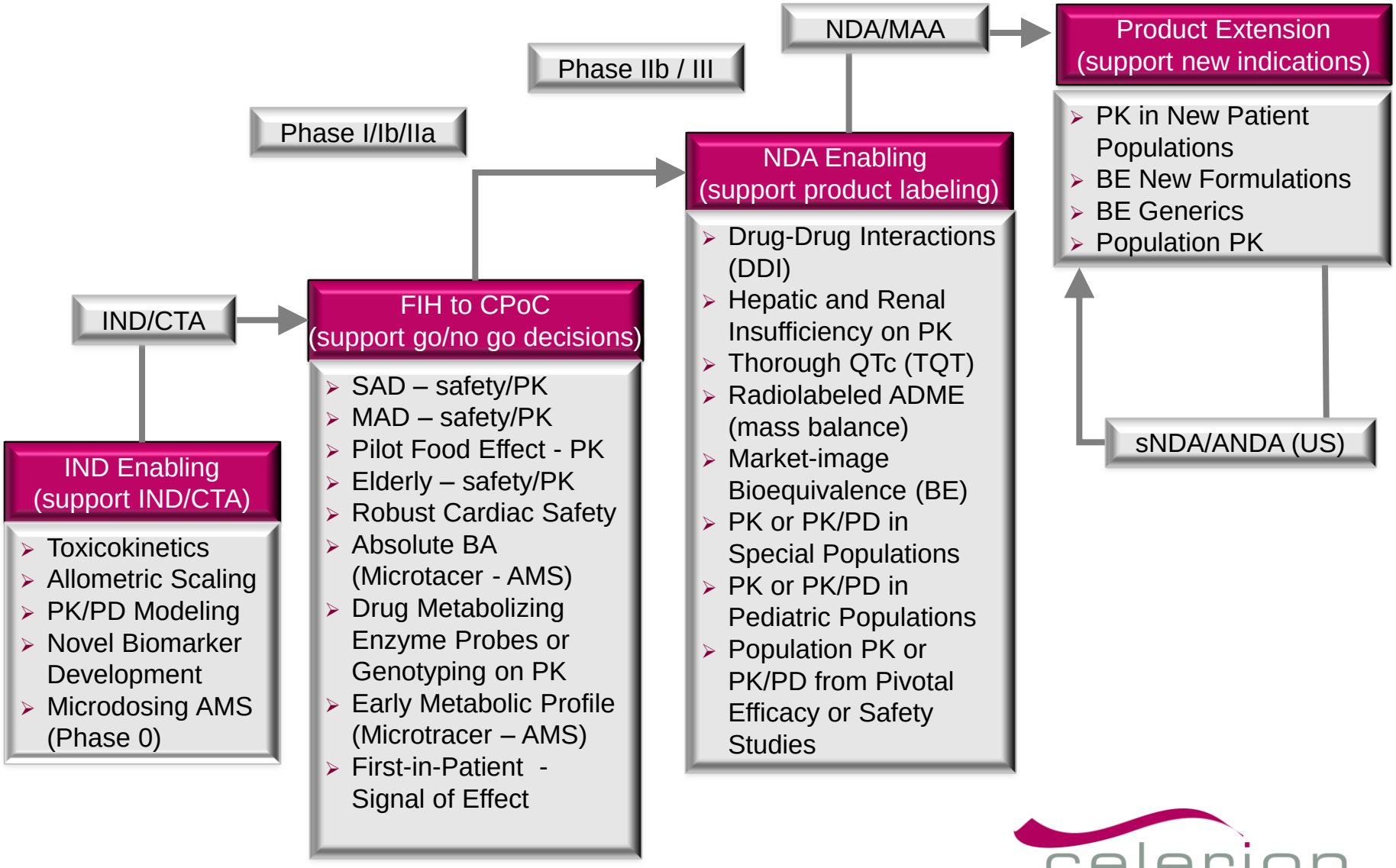
Key Questions

- Do clinical pharmacology studies require a different outsourcing model than larger late stage clinical studies?
- Are new outsourcing models needed for multi-site patient studies that require specialized clinical pharmacology services?
- What role will Europe have to play in early clinical research?
- Can strategic partnerships work to help keep up with the changing needs of early clinical research?

Clinical Pharmacology Impact Areas in Drug Development



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Clinical Pharmacology Studies Different From Confirmatory Clinical Trials

Clinical Pharmacology Phase I & IIa

- Small number of participants
- Few sites, usually single geography
- High density sampling
- Sampling logistics critical
- Specialized units with participant confinement capabilities
- Focus on “Proof-of-Presence”, “Proof-of-Mechanism”, “Proof-of-Concept” and specific product labeling needs.
- €€

Phase II/III Studies

- Large numbers of participants
- Many sites, many countries and geographies
- Low density sampling
- Study logistics critical
- Hospital or outpatient clinic settings
- Focus on pivotal efficacy and safety for regulatory approval and major product labeling claims
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Why healthy participants in Phase I?

- Provide more resilient human population if adverse events occur
  - TeGenero (2006). Starting dose: 1/500 NOAEL, 4/6 multi-organ failure in healthy male participants. What if they were patients?
- Clinical development should proceed with an incremental increase in clinical risk
  - Traditional Approach:
    Healthy participants (Phase I) → small group of patients (Phase II) → larger groups of patients (Phase III) → general patient population

What's Driving Change in Early Clinical Studies

- Fail fast in Phase I
  - More information needed for early drug development decisions
- Clinical pharmacology studies becoming more complex
  - Inclusion of patient cohorts
  - More biomarkers, more sampling
    - Sampling logistics challenges
  - Fusion and adaptive designs
  - More biologic drug candidates – immunogenicity
  - Earlier robust cardiac safety assessment

What can we learn from patients?

- Is the safety profile different in patients?
  - Consider the indication
  - Comorbidities?
  - Preclinical signals for concern?
- Is drug distribution or exposure potentially different in patients?
  - Drug metabolized or excreted by liver?
  - Drug eliminated by kidney?
- Can we get a signal (hint) of efficacy?

Signal or hint of efficacy?

- What endpoints will be used?
  - Sensitivity and variability of assessment
- Will the early clinical research study be powered to see a difference?
- What will you do with the results (if not adequately powered)? Issue a press release?
  - Kill the program?
  - Move forward?
- Biomarkers
  - Signal of target engagement
  - Signal to verify mechanism

What's Changing at Clinical Pharmacology Units

- R&D cost cutting forcing closure of in-house clinical pharmacology units at major pharma companies
- Private clinical pharmacology clinics or hybrid academic-CRO clinical pharmacology units becoming experts in innovation around robust execution
  - Hiring ex-pharma expertise
  - Building platforms for innovative technologies that provide better data, faster
  - Expertise evolves from broad experience to many situations (pay for "minds" as well as "hands")
- Global digital communications
  - Expectation of real-time data sharing and rapid digital analysis
  - Deploying smart devices in study recruitment, data capture and oversight

The Need for Global Clinical Pharmacology Unit Networks

- Most patient needs in early clinical research cannot be met by a single center
- Need to evolve similar partnering and alliance models among groups of clinical pharmacology units
  - Share patient recruiting, costs and revenues
  - Work to same quality standards (undergo common systems QA audits)
  - Valued professional relationship among PIs and/or centers
  - Coordinated through a group (CRO) which can also bring in other study services that the sponsor would need (protocol preparation, bioanalysis, PK, DM and stats, CSR preparation)

Strategic Outsourcing Phase I & IIa Studies

Benefits to Drug Developer

- Tap into expertise at specialized clinical pharmacology sites
- Benefit from growing access to specific patient populations
- Drive favorable pricing by guaranteeing volume of work to one or two suppliers
- Build trusting relationships among partnering scientific and medical staffs

Challenges for Clinical Pharmacology Services Provider

- Strategic outsourcing means different things to different drug developers
  - *Fit and philosophy on outsourcing is important*
- Trust doesn't happen overnight
  - *Builds with commitment and gradual build up of experience*
- Managing "nice-to-have" additions to protocols that have been priced to a basic economical design
- Managing mergers, changes in management and downsizing at sponsor company

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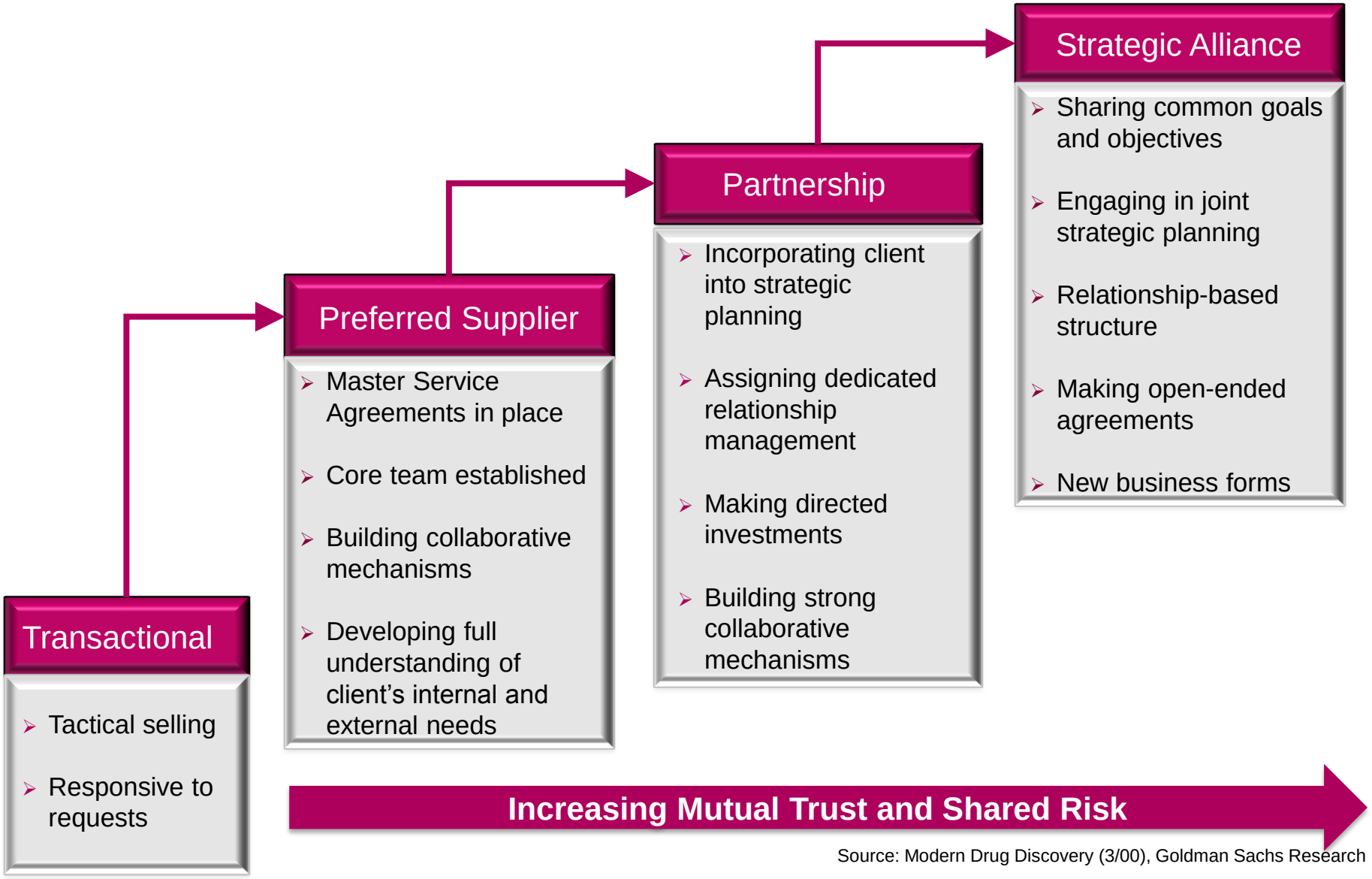
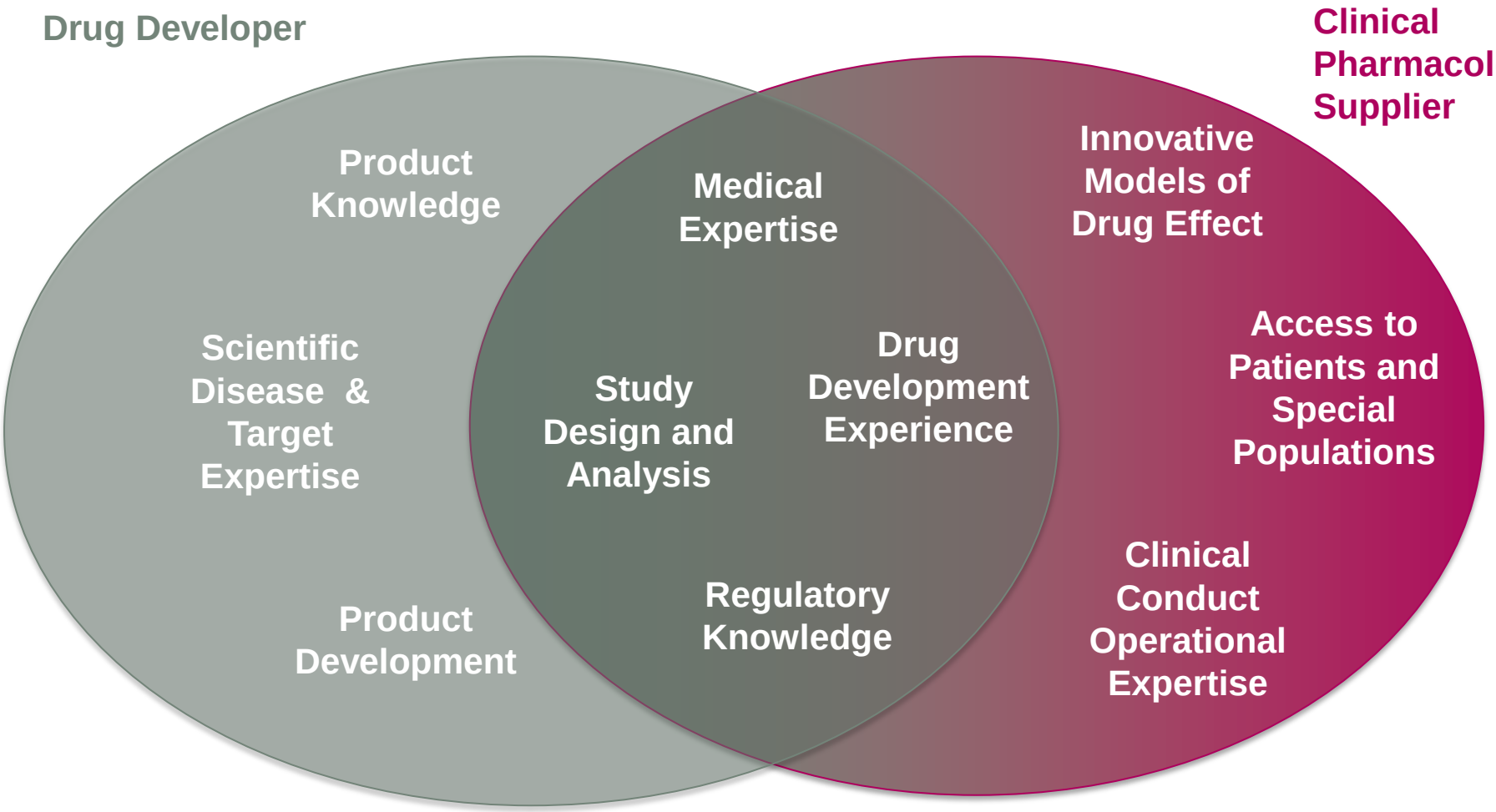
Evolution to Strategic Partnership



Source: Modern Drug Discovery (3/00), Goldman Sachs Research

Effective Partnerships Leverage Both Scientific and Operational Expertise From Each Partner



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Example of a Working Partnership

- Major Pharma client
  - Celerion had several years experience as a preferred provider among several other CROs
- Client required two or three strategic partners
  - Celerion selected as one of these after extensive evaluation process
- Novel approach to pricing specific study designs
  - Developed standard cost structure, with “a la carte” menu for optional additions
- Maintain simplicity while expanding and improving study design
  - Cost containment for client and increased study volume for Celerion
- Trust established and partnership expanded
  - Innovative partnering model developed to leverage the strengths of both organizations with elements of shared risk
- Required commitment by senior leaders on both sides
- Recognized that trust takes time to develop between both parties and evolved the expectations of partnership accordingly

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Conclusions

- Intrinsic differences between clinical pharmacology and late phase studies which need to be considered during the outsourcing process
- Build network of specialty clinics to outsource studies
  - Collaboration with experienced clinical pharmacology CRO can speed up multi-site early phase studies in patients
- Early phase clinical research is a global business
  - Europe, with its expertise in clinical pharmacology and access to patients, will have an important role to play
- Strategic partnerships can be very beneficial if both partners truly respect what each other brings to the relationship, and there is patience to allow these partnerships to evolve over time

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