The establishment and validation of novel therapeutic targets to retard progression of chronic kidney disease

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The focus of this article is to define goals and resulting action plans that can be collectively embraced by interested stakeholders to facilitate new therapeutic approaches to mitigate chronic kidney disease progression. The specific goals include identifying druggable targets, increasing the capacity for preclinical and early clinical development, broadening the availability of new therapeutic approaches, and increasing investment in the development of new therapies to limit chronic kidney disease. Key deliverables include the establishment of new regional, national, and global consortia; development of clinical trial networks; and creation of programs to support the temporary mutual movement of scientists between academia and the biotechnology and pharmaceutical sector. Other deliverables include cataloging and maintaining up-to-date records to collate progress in renal research and development, inventorying the capacity of research and clinical networks, and describing methods to ensure novel drug development.

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Current status

Therapeutic strategies that positively impact the progression of chronic kidney disease (CKD) to inevitable renal replacement therapy are lacking. In proteinuric nondiabetic chronic nephropathies, blockade of the renin-angiotensin-aldosterone system with angiotensin-converting enzyme inhibitors have delayed the onset of end-stage kidney disease, as documented in the Ramipril Efficacy in Nephropathy study.¹ In parallel, ramipril-treated patients exhibited a decrease in proteinuria that was inversely correlated with the decline of glomerular filtration rate, suggesting a nephroprotective effect of reducing protein trafficking. However, dual blockade of the renin-angiotensin-aldosterone system using an angiotensin-converting enzyme inhibitor and an angiotensin II receptor blocker or a renin inhibitor have not proved to be a solution to address the existing treatment gap due to complications of hyperkalemia and acute kidney injury.^{2,3} In the last 12 months, however, secondary analyses of the Empagliflozin Cardiovascular Outcome Event study in patients with diabetes mellitus at a high risk of cardiovascular disease and renal dysfunction have shown a decrease in CKD progression and a reduction in hard renal endpoints, albeit in small numbers of patients.⁴ The Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results study⁵ that used a glucagon-like receptor agonist in a similar population also showed renal benefit, although specific details of the renal benefit are not yet available. In the period between the positive trials of RAAS blockade and the recent trials of incretin-based therapies, there have been few phase two-four trials that

Table 1 | Recent therapeutic trials for chronic kidney disease⁶

Indication	Therapy	Status/results	Trial registration #
Diabetic nephropathy	Aldosterone receptor antagonist	Phase 2 study completed	NCT02517320
	Aliskiren (ALTITUDE)	Phase 3 study terminated due to harm ¹⁶	NCT00549757
	Anticonnective tissue growth factor antibody FG-3019	Phase 2 study terminated due to suboptimal design	NCT00913393
	Anti-transforming growth factor- β kinase antibody (LY2382770)	Phase 2 study terminated due to lack of efficacy	NCT01113801
	Bardoxolone methyl: TSUBAKI Study, BEACON	Phase 2 study recruiting	NCT02316821
		Phase 3 study terminated due to safety concerns ¹⁷	NCT01351675
	C-C chemokine receptor type 2 antagonism	Phase 2 study completed ¹⁸	NCT01447147
	Dapagliflozin	Phase 4 study recruiting	NCT02682563
	Endothelin-A antagonist Atrasentan	Phase 3 study currently recruiting	NCT01858532
	Exenatide	Phase 4 study active but not recruiting	NCT02690883
	Mineralocorticoid receptor antagonist/finerenone	Phase 2 study completed ¹⁹	NCT01874431
	Nox1/4 inhibitor (Oral GKT137831)	Phase 3 study recruiting	NCT02540993
	Phosphodiesterase 5 inhibitor	Phase 2 study completed: negative results	NCT02010242
	Pirfenidone	Phase 2 study completed ²⁰	NCT01200394
	Pyridorin	Phase 3 study recruiting	NCT02689778
	Acthar	Phase 3 study terminated due to lack of funding	NCT02156843
	Blisibimod	Phase 4 study recruiting	NCT02382523
	Bortezomib	Phase 2 and 3 study active but not recruiting	NCT02062684
	Combination immunosuppression (STOP IgA)	Phase 4 study recruiting	NCT01103778
		Phase 3 study completed: negative results and a sign of harm ²¹	NCT00554502
IgA nephropathy	Fostamatinib	Phase 2 study recruiting	NCT02112838
	Hydroxychloroquine Sulfate	Phase 4 study recruiting	NCT02765594
	Nefecon	Phase 2 study completed: reported positive outcomes	NCT01738035
	Rituximab	Phase 4 study recruiting	NCT02571842
	Rituximab	Phase 4 study completed	NCT00498368
	Steroids in IgA nephropathy (TESTING)	Study active but not recruiting, modified due to a sign of harm	NCT01560052
	Curcumin	Phase 3 study completed: results not reported	NCT01831193
	LCZ696 (UK HARP-III)	Study active but not recruiting	ISRCTN11958993
	Metformin	Phase 2 study recruiting	NCT02903511
	Octreotide LAR (ALADIN 2)	Phase 3 study active but not recruiting	NCT01377246
Proteinuric CKD	Octreotide LAR (ALADIN)	Phase 3 study competed ²²	NCT00309283
	Pioglitazone	Phase 2 study recruiting	NCT02697617
	Sirolimus	Phase 2 and 3 study terminated due to safety and efficacy concerns ²³	NCT01223755
	Tolvaptan	Phase 3 study active but not recruiting in patients with CKD stage 2–4	NCT02160145
	Tolvaptan (TEMPO 3/4)	Phase 3 study completed ^{24,25}	NCT00428948
	Water loading	Observational study completed: results not yet reported	NCT01348035
	Abatacept	Phase 3 study completed: negative results ²⁶	NCT00774852
	Acthar	Phase 3 study active but not recruiting	NCT01714817
	Anifrolumab	Phase 4 study recruiting	NCT02226341
	Atacicept	Phase 2 study recruiting	NCT02547922
Adult PKD		Phase 2 and 3 study terminated due to safety issues	NCT00573157
	Belimumab	Phase 3 study recruiting	NCT01639339
	BI-655064	Phase 2 study recruiting	NCT02770170
	Blisibimod	Phase 3 study recruiting	NCT02514967
	Etanercept	Phase 2 study terminated: perceived risk-benefit ratio for individuals with early active RA	NCT00447265
	Infliximab	Phase 2 and 3 study terminated due to failure to recruit	NCT00368264
	Obinutuzumab	Phase 2 study recruiting	NCT02550652
	Rituximab	Phase 3 study completed: negative results ²⁷	NCT00282347
		Phase 3 study recruiting (as a single agent + standard of care)	NCT01673295
		Phase 2 study recruiting (in combination with Belimumab)	NCT02260934
Lupus nephritis			NCT01773616

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Table 1 | Recent therapeutic trials for chronic kidney disease⁶ (Continued)

Indication	Therapy	Status/results	Trial registration #
Anti-neutrophil cytoplasmic antibody vasculitis	Alemtuzumab Avacopan Eculizumab	Phase 3 study recruiting (in combination with mycophenolate mofetil)	
		Phase 4 study, status unknown	NCT01405807
		Phase 3 study recruiting	NCT02994927
		Phase 2 study terminated due to failure of patient enrolment	NCT01275287
Focal segmental glomerulosclerosis	Primary: Sparsentan, Losmapimod	Phase 2 study active but not recruiting	NCT01613118
		Phase 2 completed: results not reported	NCT02000440
	Treatment resistant: Acthar, Rituximab, Abatacept	Phase 4 study recruiting	NCT02633046
		Phase 2 study active but not recruiting	NCT01573533
		Phase 2 study recruiting	NCT02592798
Alport syndrome	Steroid resistant: Fresolimumab Bardoxolone methyl	Phase 2 completed: results not reported	NCT01663591
		Phase 2/3 study recruiting	NCT03019185
	Anti-miR-21 Ramipril	Phase 2 study active but not recruiting	NCT02855268
		Phase 3 study recruiting	NCT01485978
Miscellaneous	Eculizumab in C3 GN and dense deposit disease Rituximab in relapsing idiopathic nephrotic syndrome	Phase 1 study, status unknown	NCT01221181
		Phase 3 study completed ²⁸	NCT00981838
	Pirfenidone for fibrosis in CKD	Phase 1 study completed: results not reported	NCT02408744

ALADIN, a long-acting somatostatin on disease progression in nephropathy; ALTITUDE, Aliskiren Trial in Type 2 Diabetes Using Cardiorenal Endpoints; BEACON, Bardoxolone Methyl Evaluation in Patients with Chronic Kidney Disease and Type 2 Diabetes Mellitus: the Occurrence of Renal Events; CKD, chronic kidney disease; C3 GN, C3 glomerulonephritis; LAR, long-acting release; PKD, polycystic kidney disease; RA, rheumatoid arthritis; STOP, Supportive Versus Immunosuppressive Therapy for the Treatment of Progressive IgA Nephropathy; TEMPO 3/4, Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes; TESTING, Therapeutic Evaluation of Steroids in IgA Nephropathy Global Study; TSUBAKI, The Phase II Study of Bardoxolone Methyl in Patients With Chronic Kidney Disease and Type 2 Diabetes 25.

have reached their primary endpoint and several have been stopped due to safety concerns. Although not exhaustive, Table 1 details important recent and ongoing phase 2 to 4 clinical trials in CKD, but excludes trials that involved the transplant population. This article expands on the recently published International Society of Nephrology CKD roadmap⁶ to define goals and resulting action plans that can be collectively used by interested stakeholders to facilitate new therapeutic approaches to mitigate CKD progression.

Challenges and opportunities

There are many undisputed and complex reasons why patients with CKD remain bereft of treatment options despite an uncontroversial need to develop therapeutic interventions to impact the rising global burden of CKD. There is an acknowledged lack of coordination among scientists, investors, clinical trialists, pharmaceutical companies, regulatory authorities, policy makers, and governments to develop novel strategies to reduce the burden of CKD. It is also recognized that there are region-specific causes of CKD, requiring targeted therapies to alter the initiation of injury. Coupled to this is an incomplete understanding of the underlying multifactorial pathophysiological mechanisms that lead to CKD; this is explained in part by the inherent limitations in *in vivo* and *in vitro* models that are used to study acute and chronic diseases that converge on the entity that we collectively term as CKD. CKD is not one disease but rather the result of a variety of pathophysiological insults to the kidney, which ultimately result in failure to function correlated with pathologic changes. It is conceded, however, that

once CKD is established, the mechanisms for progression may be similar, and an inclusive approach by trialists and regulatory authorities is required. Clearly, the inclination for investment in new therapies for CKD by the private sector is driven by large clinical need but is hampered by the high risk of failure, reinforced by the history of disappointing large studies and the lack of intermediate endpoints and/or biomarkers that regulatory agencies will approve.

Moreover, there are recognized gaps in our knowledge of the complications of CKD. Patients with CKD are at a high risk for cardiovascular disease yet are often and systematically excluded from cardiovascular outcome trials.⁷ Hence, the evidence base for therapies to reduce mortality in patients with CKD, which is largely driven by cardiovascular disease, is limited. Although controlling traditional risk factors has arguably not been as successful in reducing mortality in patients with kidney disease compared to patients in the general population, blood pressure control,⁸ statin use,⁹ and blockade of the renin-angiotensin aldosterone axis^{10,11} have reduced cardiovascular events. However, excess mortality in patients with CKD remains.^{12,13}

Goals

Four goals were identified as being necessary to achieve the objective of establishing and validating novel therapeutic targets to retard CKD progression (Table 2).

1. Improve the identification of “druggable” targets that are amenable to therapeutics
2. Enhance the capacity for preclinical and early clinical development

Table 2 | Action plan to develop novel therapeutic interventions to slow chronic kidney disease (CKD) progression and reduce CKD complications⁶

Goals	Activities	Partners	Possible deliverables
Improve identification of “druggable” therapeutic targets	Interrogate human samples using state-of-the art omics approaches, merged with detailed patient phenotyping and existing biomarkers to identify and qualify new therapeutic targets	Research consortia, industry, biotechnology companies, systems biologists, and geneticists	Inventory of current capacity and activities with annual updating of changes in capacity, activities, and outputs
	Enhance participation in cross-disciplinary research on pathophysiological mechanisms relevant for CKD and other diseases (e.g., fibrosis research)	Global, regional, and national societies, networks, ISN	Development of series of meetings with nonrenal scientists around areas or mechanisms (New meeting format or strategy)
	Focus academic preclinical research on the identification of “druggable” targets	Funding agencies, research networks	Number of new targets increased over current state
	Improve models of disease (animal and human) to better reflect the complexity of human CKD (e.g., AKI in the setting of CKD, CKD in the setting of vascular disease, diabetes, or metabolic syndromes)	Scientists, industry partners, biotechnology companies	Research reports
Enhance the capacity for preclinical and early clinical development	Leverage current and increase the number of effective research and clinical networks for CKD and segmented disease populations to facilitate data acquisition and trial recruitment	ISN, industry partners	Inventory of current capacity and changes over time (1–3 yr)
	Develop infrastructure to carry out state-of-the-art analyses of human tissue (CKD biopsy collections) to better understand the pathobiology of CKD and its progression		Increase the number of new agents available for specific etiologies of CKD over current agents
	Facilitate interaction and exchange of ideas between academic researchers and drug, device, and diagnostic manufacturers, with an aim to promote collaborations and mutual understanding of each other's environment and objectives	ISN, industry partners, and scientists	Development of innovative meeting formats, such as “Pitch for Partners,” as stand-alone meetings or in conjunction with major conferences
	Recognize and support academic nephrologists and kidney PhD scientists to move in and out of an industry or biotechnology research environment	Industry partners and academic institutions	1 yr and ongoing: Establishment of special scholarships to increase capacity; expanding if successful year by year
Enhance the availability of novel therapeutic approaches	Give credit to academic career development when involved in ongoing collaborations between academic and industry and biotechnology to develop therapeutics	Academic institutions and health sector, biotechnology companies, and industry partners	Policy statement at academic institutions recognizing these activities and during assessment of career development
	Evaluate opportunities for re-purposing existing drugs for diverse diseases to find treatments for CKD and its complications	Industry partners and system biologists	Workshops and conferences
	Improve access to effective but costly drugs or biologics and devices, especially in LMICs	Industry and biotechnology companies, governments, (inter-) national agencies, ministries of health, corporations, and foundations	Inventory of current availability of any therapeutics, regular update (via GKHA ¹⁸ or targeted ancillary survey) in specific LMIC 3–10 yr
	Aid from OECD countries to LMICs should be targeted for CKD prevention and treatment		

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Table 2 | Action plan to develop novel therapeutic interventions to slow chronic kidney disease (CKD) progression and reduce CKD complications⁶ (Continued)

Goals	Activities	Partners	Possible deliverables
Encourage increased investment in the development of CKD therapies	Document differences in CKD practice patterns and therapeutic needs of different countries	ISN, global, regional, and national nephrology societies	Extension of the GKHA ¹⁸ project
	Encourage industry and biotechnology and government to invest in the development of new therapies for CKD Market economic opportunity and develop business cases Evaluate opportunities for re-purposing existing drugs for diverse diseases for the treatment of CKD and its complications	As per activity Academic institutions, industry partners Industry partners and system biologists	Tailored, leveraged plans for funders, governments, WHO, World Bank, and foundations Workshop and conference

AKI, acute kidney injury; CKD, chronic kidney disease; ISN, International Society of Nephrology; LMICs, low- and middle-income countries; GKHA, Global Kidney Health Atlas; OECD, Organization for Economic Cooperation and Development; WHO, World Health Organization.

3. Broaden the availability of novel therapeutic approaches
4. Increase investment in the development of therapies to limit CKD

Activities required to deliver these goals

To achieve these ambitious goals, research consortia will need to be developed among academia, pharmaceutical and biotechnology industries, philanthropists and funding agencies, policy makers, and the government. Scientists from varied domains will need to be engaged, and clinicians across the world will require education regarding novel therapeutics to involve themselves and their patients in the necessary clinical trials to develop an evidence base required for the introduction of new therapies into clinical practice. Consortia members will inevitably be required to do things differently, as continuing with current strategies to develop new therapeutics in CKD has not been as successful as patients, clinicians, and indeed all stakeholders would expect. Hence, a focused strategy is required that is coupled with regional adaptation by high-income countries and low- and middle-income countries. The structural impediments and scientific, regulatory, legal (including protection of intellectual property), financial, risk allocation, and management silos are a formidable but not insurmountable challenge. However, with synergized effort, success should follow.

The authors identified the following actions as required to deliver the above goals (Table 2).

1. Improve the identification of targets that are amenable to therapeutics (i.e., “druggable” targets)
 - a. Focus preclinical research in academia and biotechnology and pharmaceutical sectors on the identification of “druggable” targets.
 - i. Interrogate human samples using state-of-the-art omics and other advanced microscopic and analytical approaches, merged with detailed patient phenotyping and existing biomarkers to identify and validate new therapeutic targets.
 - ii. Take full advantage of genome-wide analyses to link genetics, phenotype, and pathophysiological mechanisms to identify key drivers of renal disease; incorporate precision medicine-based approaches for target identification.
 - iii. Assess the value in preclinical studies of altering the gut microbiome through dietary strategies to improve CKD. Conduct pilot clinical studies to assess food as a potential therapy.
 - b. Improve models of disease (animal and human) to include comorbidities that better reflect the complexity of human CKD (e.g., acute kidney injury in the setting of CKD and CKD in the setting of vascular disease, diabetes, or metabolic syndrome). Compare credential preclinical models of CKD with patient samples using cutting-edge technologies (e.g., omics, NextGen sequencing, etc.) to refine or construct new models and to discover new biological pathways and targets.

- c. Generate personalized human tissue models using induced pluripotent stem cell lines with targeted mutations followed by differentiation to human kidney tissue to identify and validate “druggable” targets.
- d. Enhance participation in cross-disciplinary research on pathophysiological mechanisms relevant to CKD and other diseases (e.g., fibrosis research, immune mechanisms in chronic disease).
2. Enhance the capacity for preclinical and early clinical development
 - a. Focus on the better use of existing infrastructure to increase the number, size, and quality of clinical trials. For example, leverage research networks for CKD and segmented disease populations to facilitate data acquisition and trial recruitment.
 - b. Develop infrastructure to collect and carry out state-of-the-art analyses of human biological materials (e.g., CKD biopsy specimens) to better understand the pathobiology of CKD and its progression. Include the identification of biomarkers as predictors of disease progression and/or response to treatment. Biomarkers can also be used to define subpopulations of patients who are likely to respond to specific therapies and track this response.
 - c. Facilitate interaction and exchange of ideas between academic researchers and drug, device, and diagnostics manufacturers to promote collaborations and mutual understanding of each other’s environment and objectives.
 - d. Recognize and support academic nephrologists and PhD scientists researching the kidney to enable them to move more easily between academia and the pharmaceutical and biotechnology research environment.
 - e. Give credit to the ongoing involvement in academia and pharmaceutical and biotechnology collaborations in academic career development. Determine how best to recognize and support their engagement with the industry as traditional scholarly deliverables, including grant funding and publications, may not be forthcoming.
3. Broaden the availability of novel therapeutic approaches
 - a. Evaluate opportunities for re-purposing of existing drugs, which are currently used for diverse diseases (e.g., allopurinol, metformin), for the treatment of CKD and its complications.
 - b. Partner with biotechnology and pharmaceutical industries to assess the availability of candidate drugs developed for nonrenal indications that passed phase 1 safety studies but did not meet phase 3 primary endpoints. Determine whether these assets may impact CKD and its complications, shortening the timeline from drug discovery to clinical development.
 - c. Improve access to effective but costly drugs, biologics, and devices, especially in low- and middle-income countries. Aid from the Organization for Economic Cooperation and Development countries to low- and middle-income countries should be targeted for CKD prevention and treatment.
4. Increase investment in the development of therapies to limit CKD
 - a. Document differences in CKD practice patterns and therapeutic needs in different countries in order to leverage patient populations available for potential treatment.
 - b. Encourage pharmaceutical and biotechnology industries as well as governments to invest in the development of new therapies for CKD.
 - c. Continue to market economic opportunities and develop business cases in order to attract investors, pharmaceutical and biotechnology industries, and governments to invest in the development of new therapies for CKD.
 - d. De-risk costly and lengthy CKD trials by (i) improving patient stratification to enhance clinical success and (ii) identifying companion biomarkers that track with biological activity and efficacy and that can be independently monitored to predict clinical outcomes (death, dialysis, or change in estimated glomerular filtration rate).

Deliverables

If the above goals are achieved, ultimately, new therapies will be available to stop, slow, or reverse CKD in all populations. In the next 10 years, we defined a target goal to develop and market 10 new therapeutics in the CKD domain. Given this is a long-term outcome, intermediate deliverables are necessary (Table 2).

1. **Create multidisciplinary CKD consortia.** National, regional, and global multidisciplinary consortia consisting of members representing diverse sectors—academia, biotechnology and pharmaceutical industries, regulatory agencies, policy makers, foundations, and nonprofit organizations—can be tasked with addressing and implementing approaches to address barriers to progress in the development of treatments to diminish or arrest CKD progression. An example of an attempt to do this on a national level is the establishment of the Kidney Health Initiative in the US. This is a collaborative effort between the US Food and Drug Administration and the greater nephrology community, formed to advance kidney health, patient safety, and new therapies for renal disease. It includes stakeholders from various parts of the community, including large and small pharmaceutical companies, dialysis companies, academia, and patients to tackle issues in kidney disease. Such national or regional consortia should work together across the globe to learn from other groups and be most efficient and productive in advancing drug development.
2. **Develop clinical trial networks.** These networks can be local to a country or set of countries with a particular concentration on CKD thought to be caused by factors particularly prevalent in that region. Alternatively, these

networks can be international.¹⁴ Such networks can greatly facilitate the testing of new therapeutic agents and institutionalize “memory and experience” derived from failed and successful trials that will improve the success of future trials.

3. Programs to support the movement of academic scientists in and out of the industry and vice versa. These programs can include academic trainees or established investigators; alternatively, scientists from the pharmaceutical and biotechnology sector who are part of the drug discovery effort would benefit from being involved in renal biology and clinical nephrology in order to drive innovation that leads to new therapies.

4. Reports.

- Collate recent progress in renal research and development (e.g., new targets; development of new models or new and re-purposed agents; novel findings on the pathophysiology of CKD and its complications, etc.). Present at national and international meetings; publish research findings, including negative data that do not support successful clinical translation.
- Inventory the current capacity and activities of research networks for CKD with updating changes in capacity, activities, and outputs over time (1–3 years).
- Extend the International Society of Nephrology Global Kidney Health Atlas¹⁵ project, currently tasked to map existing resources, structures, and organizations available globally to patients with CKD and acute kidney injury, to include novel drug development.
- Leverage investment from funders, governments, and international organizations with interests in investing in low- and middle-income countries to support better health outcomes.

5. Educational and collaborative activities.

- Conduct multidisciplinary scientific meetings on targets and therapeutics, new or re-purposed, to draw on the collective experience of other disciplines (nonrenal) that have pursued diverse chronic diseases and have succeeded in clinical translation.
- Organize meetings to address barriers and solutions that hinder therapeutic success in order to broaden the cooperation and collaboration between commercial endeavors and academia.
- Promote collaborative efforts with existing consortia to better use the available data, resources, biomaterials, etc. for drug discovery and clinical development.
- Obtain policy statements from academic institutions that recognize engagement with the commercial sector as being meritorious for career advancement.

6. “Pitch for Partners” meetings among academic nephrologists, scientists, pharmaceuticals and biotechnology industries.

These meetings will allow worldwide access to key opinion leaders in order to facilitate interaction and the exchange of ideas to collectively define optimal strategies for programs in

drug and clinical development. “Pitch for Partners” can be advanced either as a stand-alone meeting or in conjunction with major conferences.

Conclusion

In order to introduce new therapeutic agents to patients with kidney disease, there are many factors that need consideration beyond the development and validation of novel targets. Medicine has seen the introduction of many new therapeutics encompassing small molecules, antibodies, DNA, and RNA therapeutics. In addition, novel approaches to improve targeted bioavailability reduce side effects and enhance efficacy, making drug delivery systems of complementary importance to the identification of novel targets. Although the focus has been on scientific development, many of the challenges in developing novel therapeutics relate to identifying project funding sources; finding suitable contract manufacturing companies that are Good Manufacturing Practice compliant; and protecting intellectual property generated from scientific advances while maintaining essential collaboration. Taxation and regulatory policies, including offering patent exclusivity and expedited review for breakthrough therapies for CKD, should provide incentives to develop innovative therapeutics in CKD. Trials with the aim of re-purposing of generic therapeutics should be prioritized if sufficient scientific evidence is available. Furthermore, strategies used to extend patent life of drugs, but without investment to assess re-purposing, should be discouraged. Finally, if the above goals are achieved, new therapies will certainly become available to stop, slow, or reverse CKD. Most importantly, these therapies should be made accessible to populations around the globe.

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