

Р†РќРЎРЎР РЈРЉРІР†РЇ

**PrP»CЦ PjPμPrPëC±PSPsPiPs P•P°CÍC,PsCÍCřPIP°PSPSCЦ P»C-PeP°CЦCÍCHPePsPiPs
P•P°CÍPsP±Cř**

P'P†P'PℏP™P Pℏ

$P\check{Y}P\in P\gg P^\circ P\Gamma$:

$$PrC-C\bar{H}C\ddagger P^{\circ} \ C\bar{H}P\mu C\ddagger PsPIP\ddot{e}PSP^{\circ}: \ C\acute{r}P\ddot{e}P\gg PrP\mu PSP^{\circ}C,,C-P\gg C\acute{r} \ C\ddagger P\ddot{e}C,C\bar{H}P^{\circ}C,,$$

1 C,P°P±P»PµC,PεP° P¶CřPIP°P»CHßPSP° PjC-CřC,PëC,CH CřPëP»PrPµPSP°C,,C-P»Cř 50 PjPi Cř C,,PsCßPjC- CřPëP»PrPµPSP°C,,C-P»Cř C†PëC,CßP°C,Cř 70,24 PjPi P°P±Ps

1 C,P°P±P»P_μC,P_eP° P¶C_rPIP°P»CH₅PSP° P_jC-C_rC,P_eC,CH₅ C_rP_eP»PrP_μPSP°C_„,C-P»C_r 100 P_jP_i C_r C_„,P_sC₇P_jC- C_rP_eP»PrP_μPSP°C_„,C-P»C_r C_rP_eC,C₇P°C,C_r 140,48 P_jP_i;

*PrPsPiPsPjC-P¶PSC- C¶PµC¶PsPIPëPSPë: PeP°P»C-Ç¶ PiPsP»P°PeC¶PëP»C-PS; PjP°PiPSC-Ç¶ C¶C, PµP°C¶P°C,; PeC¶PµPjPSC-Ç¶ PrC-PsPeC¶PëPr PePsP»PsC-PrPSPëP¶
P±PµP·PiPsPrPSPëP¶; P°C¶PiP°C¶C,P°Pj (P· 951); PSP°C,C¶C-Ç¶
PeC¶PsC¶PeP°C¶PjPµP»PsP·P°; P°C¶PsPjP°C,PëP·P°C,PsC¶ PjB¶™ C¶C,P° PiPµC¶C†PµPIP°;
P»P°PeC,PsP·P°, PjPsPSPsPiC-PrC¶P°C,; PiPsPIC-PrPsPS P¶-30.*

$$\text{P}^{\circ}\text{C}-\text{PeP}^{\circ}\text{C}\dot{\text{H}}\text{C}\dot{\text{H}}\text{C}\text{H}\text{PeP}^{\circ}\text{C}_{\text{H}}\text{PsC}\dot{\text{H}}\text{PjP}^{\circ}\text{. PyP}^{\circ}\text{P}\pm\text{P}\gg\text{P}_{\text{H}}\text{C,PeP}\ddot{\text{e}}\text{P}\|\text{C}\dot{\text{r}}\text{PIP}^{\circ}\text{P}\gg\text{CH}\text{PSC}\text{.}$$

PhCl'PSPsPIPSC- C,,C-P·PëPePs-C...C-PjC-C±PSC- PIP»P°Cl'C,PëPIPsCl'C,C-: C,CḡPëPeCrC,PSC- PrPIPsPsPïCrPeP»C- C,P°P±P»PuC,PePë P±C-P»PsPiPs PePsP»CHbPsCḡCr P· C,PëCl'PSPuPSPSClḡj B«50B» P°P±Ps B«100B» P· PsPrPSPsPiPs P±PsPeCr.

[illegible]

$P \rightleftharpoons P^{\circ} C \bar{H} P j P^{\circ} P e P s P \gg P s P i C - C \nmid P S C - P I P \gg P^{\circ} C \bar{I} C, P \ddot{e} P I P s C \bar{I} C, C - .$

$$P \propto P^\circ C \bar{h} P j P^\circ P \epsilon P s P \tau P \ddot{e} P S P^\circ P j C - P \epsilon P^\circ.$$

PŸPĖP»PrPµPSP°C„C-P» вѣ“ PĭCĥPµPĭP°CĥP°C, PrP»Cĭ PĭPµCĥPsCĥP°P»CĥPSPsPiPs
 P·P°CĭC,PsCĭCĭPIP°PSPSCĭ, PĭCĥPĖP·PSP°C‡PµPSPĖPN» PrP»Cĭ P»C-PeCĭPIP°PSPSCĭ
 PµCĥPµPeC,PĖP»CĥPSPsC— PrPĖCĭC„CĭPSPeC‡C— . PµCĥPĖ CĭPµPeCĭCĭP°P»CĥPSPsPjCĭ
 P·P±CĭPrP¶PµPSPSC- PĭCĥPµPĭP°CĥP°C, PIC-PrPSPsPIP»CĥC” P·PSPĖP¶PµPSCĭ
 PµCĥPµPeC,PĖP»CĥPSCĭ C„CĭPSPeC‡C-Cĥ CĖP»CĭC...PsPj PĭPsCĭPĖP»PµPSPSCĭ
 PĭCĥPĖC,PsPeCĭ PeCĥPsPIC- PrPs CĭC,P°C,PµPIPsPiPs C‡P»PµPSP°.

PαC-P·C-PsP»PsPiC-C‡PSPëPNë PjPμC...P°PSC-P·Pj, C%Ps P·CfPjPsPIP»CñC" PμCñPμPeC‡C-Cñ,
PIPeP»CñC‡P°C" PIPëPIC-P»CHbPSPμPSPSC‡ PsPeC‡PëPrCf P°P·PsC,Cf (NO) Cf
PeP°PIPμCñPSPsP·PSPëC... C,C-P»P°C... PìC-Pr C‡P°C‡ C‡PμPeC‡CfP°P»CHbPSPsPiPs
P·P±CfPrP¶PμPSPSC‡. P'PëPIC-P»CHbPSPμPSPëPNë NO P°PeC,PëPICfC" C,,PμCñPjPμPSC,
PiCfP°PSC-P»P°C,C‡PëPeP»P°P·Cf, C%Ps C‡C,PëPjCfP»CñC" PìC-PrPIPëC%PμPSPSC‡
CñC-PIPSC‡ C‡PëPeP»C-C‡PSPsPiPs PiCfP°PSPsP·PëPSPjPsPSPsC,,PsC‡C,,P°C,Cf (C‡P"PhPα),
PIPëPeP»PëPeP°C" CñPsP·C‡P»P°P±P»PμPSPSC‡ PiP»P°PrPePsC— PjCfC‡PeCfP»P°C,CfCñPë
PeP°PIPμCñPSPsP·PSPëC... C,C-P» C,P° C‡PìCñPëC‡C" PìCñPëC,PsPeCf PeCñPsPIC-.

PŸPëP»PrPμPSP°C,,C-P» C" PìPsC,CfP¶PSPëPj C,P° C‡PμP»PμPeC,PëPIPSPëPj
C-PSPiC-P±C-C,PsCñPsPj C‡P"PhPα-C‡PìPμC‡PëC,,C-C‡PSPsC—
C,,PsC‡C,,PsPrC-PμC‡C,PμCñP°P·PëB B B B B B B 5 (PαP"P·5) Cf PeP°PIPμCñPSPsP·PSPëC...
C,C-P»P°C..., PrPμ PαP"P·5 PIC-PrPìPsPIC-PrP°C" P·P° CñPsP·PìP°Pr C‡P"PhPα. P·C,,PμPeC,Pë
C‡PëP»PrPμPSP°C,,C-P»Cf PSP° PμCñPμPeC‡C-Cñ PjP°CñC,CHb PìPμCñPëC,,PμCñPëC‡PSPëPNë
C...P°CñP°PeC,PμCñ. PŸPëP»PrPμPSP°C,,C-P» PSPμ C‡PëPSPëC,CHb
P±PμP·PìPsC‡PμCñPμPrPSCñPsC— CñPμP»P°PeC‡P°C‡C-PNëPSPsC— PrC-C— PSP°
C-P·PsP»CHbPsPIP°PSC- PeP°PIPμCñPSPsP·PSC- C,C-P»P° P»CñPrPëPSPë, P°P»Pμ
PìPsC,CfP¶PSPs PìPsC‡PëP»CñC" CñPsP·C‡P»P°P±P»CñPIP°P»CHbPSCf PrC-Cñ NO PSP° C‡Cñ
C,PeP°PSPëPSCf. PμCñPë P°PeC,PëPIP°C‡C-C— PjPμC,P°P±PsP»C-C‡PSPsPiPs CëP»C‡C...Cf
NO/C‡P"PhPα, C%Ps PIC-PrP±C‡PIP°P°C,CñC‡C‡ PìCñPë C‡PμPeC‡CfP°P»CHbPSC-PNë
C‡C,PëPjCfP»C‡C‡C-C—, C-PSPiC-P±C‡PIP°PSPSC‡ C‡PëP»PrPμPSP°C,,C-P»PsPj PαP"P·5
C‡PìCñPëC‡PëPSC‡C" PìC-PrPIPëC%PμPSPSC‡ CñC-PIPSC‡ C‡P"PhPα Cf
PeP°PIPμCñPSPsP·PSPëC... C,C-P»P°C.... PŸP°PePëPj C‡PëPSPsPj, PrP»C‡C,C,PsPiPs, C%PsP±
PìC-C‡P»C‡C P·P°C‡C,PsC‡C‡PIP°PSPSC‡ C‡PëP»PrPμPSP°C,,C-P»Cf PIPëPSPëPe
PSPμPsP±C...C-PrPSPëPNë C,,P°CñPjP°PePsP»PsPiC-C‡PSPëPNë PμC,,PμPeC,,
PSPμPsP±C...C-PrPSPμ C‡PμPeC‡CfP°P»CHbPSPμ P·P±CfPrP¶PμPSPSC‡.

P"PsC‡P»C-PrP¶PμPSPSC‡ in vitro PìCñPsPrPμPjPsPSC‡C,CñCfPIP°P»Pë, C%Ps
C‡PëP»PrPμPSP°C,,C-P» C" C‡PμP»PμPeC,PëPIPSPëPj PrPs PαP"P·5, C%Ps P±PμCñPμ
P°PeC,PëPIPSCf C‡C‡P°C‡C,CHb Cf PìCñPsC‡PμC‡C- PμCñPμPeC‡C-C—. P·C,,PμPeC,
C‡PëP»PrPμPSP°C,,C-P»Cf PSP° PαP"P·5 PìPsC,CfP¶PSC-CëPëPNë, PSC-P¶ PSP° C-PSCëC-
PIC-PrPsPjC- C,,PsC‡C,,PsPrC-PμC‡C,PμCñP°P·Pë. PìPμPNë PμC,,PμPeC, Cf 10 CñP°P·C-PI
PìPsC,CfP¶PSC-CëPëPNë, PSC-P¶ PμC,,PμPeC, PSP° PαP"P·6, C%Ps P±PμCñPμ C‡C‡P°C‡C,CHb Cf
PìCñPsC‡PμC‡P°C... C,,PsC,PsPìPμCñPμC,PIPsCñPμPSPSC‡ Cf C‡C-C,PeC-PIC‡C-. PμCñPë
P·P°C‡C,PsC‡C‡PIP°PSPSC- PjP°PeC‡PëPjP°P»CHbPSPëC... CñPμPePsPjPμPSPPrPsPIP°PSPëC...
PrPsP· C‡PμP»PμPeC,PëPIPSC-C‡C,CHb C‡PëP»PrPμPSP°C,,C-P»Cf PrPs PαP"P·5 Cf 80
CñP°P·C-PI PìPμCñPμPIPëC%C‡C" PNëPsPiPs C‡PμP»PμPeC,PëPIPSC-C‡C,CHb PrPs PαP"P·1, Cf
700 CñP°P·C-PI PIPëC%P°, PSC-P¶ PrPs PαP"P·2, PαP"P·3, PαP"P·4, PαP"P·7, PαP"P·8,
PαP"P·9, PαP"P·10 C,P° PαP"P·11. P—PsPeCñPμPjP°, C‡PμP»PμPeC,PëPIPSC-C‡C,CHb
C‡PëP»PrPμPSP°C,,C-P»Cf PrPs PαP"P·5 Cf 4000 CñP°P·C-PI PìPμCñPμPIPëC%C‡C" PNëPsPiPs
C‡PμP»PμPeC,PëPIPSC-C‡C,CHb PrPs PαP"P·3 бñ" C‡PñPhPα-C‡PìPμC‡PëC,,C-C‡PSPsC—
C-P·PsC,,PsCñPjPë C,,PsC‡C,,PsPrC-PμC‡C,PμCñP°P·Pë, C%Ps P±PμCñPμ C‡C‡P°C‡C,CHb Cf
CñPμPiCfP»C‡C‡C-C— C‡PμCñC‡PμIPsC— C‡PePsCñPsC,P»PëIPsC‡C,C-.

PαP°CñPjP°PePsPeC-PSPμC,PëPeP°.

PñP±C‡PsCñP±C‡C-C‡C. PŸPëP»PrPμPSP°C,,C-P» CëPIPëPrPePs P°P±C‡PsCñP±C‡C"C,CHbC‡C‡C.
PhP°PeC‡PëPjP°P»CHbPSC- PìP»P°P·PjPsPIC- PePsPSC‡PμPSC,CñP°C‡C-C— PìCñPμPìP°CñP°C,Cf
PrPsC‡C‡PìP°CñC,CHbC‡C‡C PìCñPsC,C‡PiPsPj 30бñ"120 C...PIPëP»PëPS (C-P·
PjPμPrC-P°PSPsCñ 60 C...PIPëP»PëPS) PìC-C‡P»C‡C PNëPsPiPs PìPμCñPsCñP°P»CHbPSPsPiPs
P·P°C‡C,PsC‡C‡PIP°PSPSC‡ PSP°C,C%Pμ. PŸPμCñPμPrPSC‡ P°P±C‡PsP»CñC,PSP°
P±C-PsPrPsC‡C,CfPìPSC-C‡C,CHb PìC-C‡P»C‡C PìPμCñPsCñP°P»CHbPSPsPiPs

P·P°CfC,PsCfCfPIP°PSPSCf CfC,P°PSPsPIPëC,CH 41 % (C-P· PrC-P°PïP°P·PsPSPsPj
P·PSP°CfPµPSCf PIC-Pr 25 PrPs 63 %). Pj CfPµPePsPjPµPSPPrPsPIP°PSPsPjCf
PrC-P°PïP°P·PsPSC- PrPsP· (PIC-Pr 25 PrPs 100 PjPi) PïP»PsC%°P° PïC-Pr
C„P°CfPjP°PePsPeC-PSPµC,PëCfPSPsCf PeCfPëPIPsCf B«PePsPSCfPµPSC,CfP°CfC-Cf-
CfP°CfB» (AUC) C,P° PjP°PeCfPëPjP°P»CHPSP° PePsPSCfPµPSC,CfP°CfC-Cf (PŸ_{max})
CfPëP»PrPµPSP°C„C-P»Cf PïC-CfP»Cf PµPsPiPs PïPµCfPsCfP°P»CHPSPsPiPs
P·P°CfC,PsCfCfPIP°PSPSCf PïC-PrPIPëC%°CfCfC,CHCfCf PïCfPsPiPsCfCfC-PµPSPs PrPs
PrPsP·Pë.

PµCfPë P·P°CfC,PsCfCfPIP°PSPSC- CfPëP»PrPµPSP°C„C-P»Cf PïC-Pr CfP°Cf
PIP¶PëPIP°PSPSCf C—P¶C- CfC,CfPïC-PSCH P°P±CfPsCfP±CfC-C— P·PSPëP¶CfC”C,CHCfCf
P·C- CfPµCfPµPrPSC-Pj PïPsPrPsPIP¶PµPSPSCfPj CfP°CfCf PrPsCfCfPiPSPµPSPSCf
PjP°PeCfPëPjP°P»CHPSPsC— PePsPSCfPµPSC,CfP°CfC-C— (T_{max}) PrPs 60 C...PIPëP»PëPS C-
CfPµCfPµPrPSC-Pj P·PSPëP¶PµPSPSCfPj C_{max} PSP° 29 %.

P PsP·PïPsPrC-P». PŸPµCfPµPrPSC-Pµ CfC-PIPSPsPIP°P¶PSPëPµ PsP±Bf™ C”Pj
CfPsP·PïPsPrC-P»Cf (V_d) CfC,P°PSPsPIPëC,CH 105 P»C-C,CfC-PI, C%°Ps CfPIC-PrCfPëC,CH
PïCfPs CfPsP·PïPsPrC-P» PïCfPµPïP°CfP°C,Cf PI C,PeP°PSPëPSP°C... PsCfPiP°PSC-P·PjCf.
PµC-CfP»Cf PsPrPSPsCfP°P·PsPiPsPiPs PïPµCfPsCfP°P»CHPSPsPiPs
P·P°CfC,PsCfCfPIP°PSPSCf CfPëP»PrPµPSP°C„C-P»Cf PI PrPsP·C- 100 PjPi CfPµCfPµPrPSCf
PjP°PeCfPëPjP°P»CHPSP° P·P°PïP°P»CHPSP° PïP»P°P·PjPsPIP° PePsPSCfPµPSC,CfP°CfC-Cf
CfPëP»PrPµPSP°C„C-P»Cf CfC,P°PSPsPIPëC,CH PïCfPëP±P»PëP·PSPs 440 PSPi/PjP»
(PePsPµC„C-CfC-C”PSC, PIP°CfC-P°CfC-C— CfC,P°PSPsPIPëC,CH 40 %). PhCfPeC-P»CHPePë
P·PiBf™ CfP·CfPIP°PSPSCf CfPëP»PrPµPSP°C„C-P»Cf C,P° PµPsPiPs PiPsP»PsPiPSPsPiPs N-
PrPµCfPjPµC,PëP»PjPµC,P°P±PsP»C-C,Cf P· P±C-P»PeP°PjPë PïP»P°P·PjPë PeCfPsPIC-
PrPsCfCfPiP°C” 96 %, CfPµCfPµPrPSCf PjP°PeCfPëPjP°P»CHPSP° PïP»P°P·PjPsPIP°
PePsPSCfPµPSC,CfP°CfC-Cf PIC-P»CHPSPsPiPs CfPëP»PrPµPSP°C„C-P»Cf PrPsCfCfPiP°C” 18
PSPi/PjP» (38 PSPjPsP»CH). PŸC,CfPïC-PSCH P·PiBf™ CfP·CfPIP°PSPSCf P· P±C-P»PeP°PjPë
PïP»P°P·PjPë PeCfPsPIC- PSPµ P·P°P»PµP¶PëC,CH PIC-Pr P·P°PïP°P»CHPSPëC...
PePsPSCfPµPSC,CfP°CfC-Pµ CfPëP»PrPµPSP°C„C-P»Cf.

Pj P·PrPsCfPsPIPëC... PrPsP±CfPsPiPsP»CHCfC-PI, CfPeC- P·P°CfC,PsCfPsPICfPIP°P»Pë
CfPëP»PrPµPSP°C„C-P» PsPrPSPsCfP°P·PsPiPs PI PrPsP·C- 100 PjPi, CfPµCfPµP·
90 C...PIPëP»PëPS PI PµCfPeCfP»CfC,C- PIPëP·PSP°CfP°P»PsCfCf PjPµPSCfPµ 0,0002 % (Cf
CfPµCfPµPrPSCfPsPjCf 188 PSPi) P·P°CfC,PsCfPsPIP°PSPsC— PrPsP·Pë.

P’C-PsC,CfP°PSCfC„PsCfPjP°CfC-Cf. PµPµC,P°P±PsP»C-P·Pj CfPëP»PrPµPSP°C„C-P»Cf
PIC-PrP±CfPIP°C”C,CHCfCf PiPsP»PsPiPSPëPj CfPëPSPsPj P·P° CfCfP°CfC,CH
PjC-PeCfPsCfPsPjP°P»CHPSPëC... C-P·PsC„PµCfPjPµPSC,C-PI PïPµCfC-PSPëPë CYP3A4
(PiPsP»PsPiPSPëPµ CëP»CfC...) C,P° CYP2C9 (PrCfCfPiPsCfCfPrPSPëPµ CëP»CfC...)
P”PsP»PsPiPSPëPµ CfPëCfPeCfP»CfCfCfPëPµ PjPµC,P°P±PsP»C-C,
CfC,PIPsCfCfC”C,CHCfCf CëP»CfC...PsPj N-PrPµPjPµC,PëP»CHPIP°PSPSCf
CfPëP»PrPµPSP°C„C-P»Cf. PŸPµP»PµPeC,PëPIPSC-CfC,CH PjPµC,P°P±PsP»C-C,Cf C%°PsPrPs
PµP”P·5 PïPsCfC-PIPSCfPSPSP° P·C- CfPµP»PµPeC,PëPIPSC-CfC,Cf
CfPëP»PrPµPSP°C„C-P»Cf, P° P°PeC,PëPIPSC-CfC,CH PjPµC,P°P±PsP»C-C,Cf C%°PsPrPs
PµP”P·5 CfC,P°PSPsPIPëC,CH PïCfPëP±P»PëP·PSPs 50 % P°PeC,PëPIPSPsCfC,C-
PIPëC...C-PrPSPsC— CfPµCfPsPiPëPSPë. PµP»P°P·PjPsPIC- PePsPSCfPµPSC,CfP°CfC-C—
CfCHPsPiPs PjPµC,P°P±PsP»C-C,Cf CfC,P°PSPsPIP»CfC,CH PïCfPëP±P»PëP·PSPs 40 %
PePsPSCfPµPSC,CfP°CfC-C— CfPëP»PrPµPSP°C„C-P»Cf Cf PïP»P°P·PjC- PeCfPsPIC-. N-
PrPµPjPµC,PëP»CHPsPIP°PSPëPµ PjPµC,P°P±PsP»C-C, P·P°P·PSP°C” PïPsPrP°P»CHCëPsPiPs
PjPµC,P°P±PsP»C-P·PjCf, P° PïPµCfC-PsPr PµPsPiPs PSP°PïC-PIPIPëPIPµPrPµPSPSCf

СГГ,Р°PSPsPIPëC,CH ПГГПëP±P»PëP·PSPs 4 PiPsPrPëPSPë.

Р'PëPIPrPµPSPSCЦ. Р—Р°PiP°P»CHPSPëPNë PeP»C-ГГРµPSCГГ ГГ'PëP»PrPµPSP°C,,C-P»Cr
СГГ,Р°PSPsPIPëC,CH 41 Р»/PiPsPr, Р·CrPjPsPIP»CHCHC±Pë PiPµГГC-Pr PNëPsPiPs
PSP°PiC-PIPIPëPIPrPµPSPSCЦ C,ГГПëPIP°P»C-СГГ,CH 3БГ "5 PiPsPrPëPS. ПГPe PiC-ГГ'P»ЦЦ
PiPµГГPsГГР°P»CHPSPsPiPs, C,Р°Pe C- PiC-ГГ'P»ЦЦ PIPSCГГ,ГГC-СëPSCHPsPIPrPµPSPSPsPiPs
Р·Р°СГГ,PsСГГCrPIP°PSPSCЦ РµPeСГГPeГГРµCГC-ЦЦ ГГ'PëP»PrPµPSP°C,,C-P»Cr Cr
PIPëPiP»ЦЦPrC- PjPµC,Р°P±PsP»C-C,С-PI Р·PrC-PNëСГГPSCГГC,CHCГГЦЦ PiPsP»PsPIPSPëPj
C±PëPSPsPj C-Р· PeP°P»PsPj (PiГГПëP±P»PëP·PSPs 80 % PIPIPrPµPSPsC—
PiPµГГPsГГР°P»CHPSPsC— PrPsP·Pë) C,Р° PjPµPSCëPsCH PjC-ГГPsCH Р·C- ГГ'PµC±PµCH
(PiГГПëP±P»PëP·PSPs 13 % PIPIPrPµPSPsC— PiPµГГPsГГР°P»CHPSPsC— PrPsP·Pë).

РµР°ГГPjР°PePsPeC-PSPµC,PëPeP° Cз PsСГГPs±P»PëPIPëC... PiГГCзPi PiP°CГC-C"PSC,C-PI.

РµР°CГC-C"PSC,Pë Р»C-C,PSCHPsPiPs PIC-PeCr. Pj Р·PrPsГГPsPIPëC...
PrPsP±ГГPsPIPsP»CHCГC-PI Р»C-C,PSCHPsPiPs PIC-PeCr (PIC-PePsPj PIC-Pr 65 ГГPsPeC-PI)
PIC-PrP·PSP°C±P°P»PsСГГЦЦ Р·PSPëP¶PµPSPSCЦ PeP»C-ГГРµPSCГГCr
ГГ'PëP»PrPµPSP°C,,C-P»Cr, C%Ps Р·CrPjPsPIP»CHPIP°P»Ps PiC-PrPIPëC%PµPSPSCЦ
PiP»P°P·PjPsPIPëC... PePsPSCГPµPSC,ГГР°CГC-PNë ГГ'PëP»PrPµPSP°C,,C-P»Cr C,Р° PNëPsPiPs
Р°PeC,PëPIPSPsPiPs N-PrPµPjPµC,PëP»CHPsPIP°PSPsPiPs PjPµC,Р°P±PsP»C-C,Cr
PiГГПëP±P»PëP·PSPs PSP° 90 % PiPsГГC-PIPSCЦPSPs Р· PIC-PrPiPsPIC-PrPSPëPjPë
PePsPSCГPµPSC,ГГР°CГC-ЦЦPjPë Cr Р·PrPsГГPsPIPëC... PrPsP±ГГPsPIPsP»CHCГC-PI
PjPsP»PsPrCëPsPiPs PIC-PeCr (18БГ "45 ГГPsPeC-PI). Pj Р·PiБГ™ ЦЦP·PeCr Р· PIC-PePsPIPëPjPë
PIC-PrPjC-PSPSPсГГC,ЦЦPjPë Cr Р·PiБГ™ ЦЦP·CrPIP°PSPSC- Р· P±C-P»PeP°PjPë PiP»P°P·PjPë
PeГГPsPIC- PIC-PrPiPsPIC-PrPSPµ PiC-PrPIPëC%PµPSPSCЦ PiP»P°P·PjPsPIPsC—
PePsPSCГPµPSC,ГГР°CГC-C— PIC-P»CHPSPsPiPs ГГ'PëP»PrPµPSP°C,,C-P»Cr
СГГ,Р°PSPsPIPëP»Ps PiГГПëP±P»PëP·PSPs 40 %.

РкPëГГPePsPIP° PSPµPrPsСГГ,Р°C,PSC-СГГ,CH. Pj PrPsP±ГГPsPIPsP»CHCГC-PI C-P·
PiPsГГCrCëPµPSPSCЦPjPë C,,CrPSPeCГC-C— PSPëГГPsPe Р»PµPiPePsPiPs C,Р°
PiPsPjC-ГГPSPsPiPs СГГ,CrPiPµPSCЦ (PeP»C-ГГРµPSCГГ PeГГРµP°C,PëPSC-PSCr 30БГ "80
PjP»/C...PI) C,,Р°ГГPjР°PePsPeC-PSPµC,PëPeP° ГГ'PëP»PrPµPSP°C,,C-P»Cr
Р·Р°P»PëCëP°P»Р°СГГЦЦ PSPµP·PjC-PSPµPSPsCH PiC-ГГ'P»ЦЦ PNëPsPiPs
PsPrPSPsГГР°P·PsPIPsPiPs PiPµГГPsГГР°P»CHPSPsPiPs Р·Р°СГГ,PsСГГCrPIP°PSPSCЦ Cr
PrPsP·C- 50 PjPi. PÿPµГГРµPrPSC- AUC C,Р° C_{max} N-PrPµPjPµC,PëP»CHPsPIP°PSPsPiPs
PjPµC,Р°P±PsP»C-C,Cr PiC-PrPIPëC%CrPIP°P»PëСГГЦЦ PSP° 126 % C,Р° 73 %
PIC-PrPiPsPIC-PrPSPs PiPsГГC-PIPSCЦPSPs Р· C,Р°PePëPjPë PiPsPeP°P·PSPëPeP°PjPë Cr
PrPsP±ГГPsPIPsP»CHCГC-PI C,Р°PePsPiPs P¶ PIC-PeCr P±PµP· PiPsГГCrCëPµPSCH
C,,CrPSPeCГC-C— PSPëГГPsPe. PhPrPSP°Pe C±PµГГРµP· PIPëСГГPsPeCr
C-PSPPrPëPIC-PrCrP°P»CHPSCr PIP°ГГC-Р°P±PµP»CHPSC-СГГ,CH CГC-
PIC-PrPjC-PSPSPсГГC,C- PSPµ P±CrP»Pë СГГ,Р°C,PëСГГ,PeC±PSPs Р·PSP°C±CrC%PëPjPë.

Pj PrPsP±ГГPsPIPsP»CHCГC-PI C-Р· C,ЦЦP¶PePëPjPë PiPsГГCrCëPµPSPSCЦPjPë
C,,CrPSPeCГC-C— PSPëГГPsPe (PeP»C-ГГРµPSCГГ PeГГРµP°C,PëPSC-PSCr PSPëP¶C±Pµ 30
PjP»/C...PI) PeP»C-ГГРµPSCГГ ГГ'PëP»PrPµPSP°C,,C-P»Cr Р·PSPëP¶CrPIP°PICГГЦЦ, C%Ps
СГГPiГГPëC±PëPSCЦP»Ps ГГ'PµГГРµPrPSC" PiC-PrPIPëC%PµPSPSCЦ AUC C,Р° C_{max} PSP° 100 %
C,Р° 88 % PIC-PrPiPsPIC-PrPSPs PiPsГГC-PIPSCЦPSPs C-Р· PrPsP±ГГPsPIPsP»CHCГCЦЦPjPë
C,Р°PePsPiPs P¶ PIC-PeCr P±PµP· PiPsГГCrCëPµPSCH C,,CrPSPeCГC-C— PSPëГГPsPe.
РлГГC-Pj C,PsPiPs, Р·PSP°C±PµPSPSCЦ AUC C,Р° C_{max} N-PrPµPjPµC,PëP»CHPsPIP°PSPsPiPs
PjPµC,Р°P±PsP»C-C,Cr Р·PSP°C±CrC%Pµ PiC-PrPIPëC%CrPIP°P»PëСГГЦЦ БГ " PSP° 200 % C,Р°
79 % PIC-PrPiPsPIC-PrPSPs.

- PŸC,P°PSPë, PìCĤPë CĬPePëC... PSPμ CĤPμPePsPjPμPSPPrPsPIP°PSP°
CĬPμPeCĬCĬP°P»CHBPSP° P°PeC,PëPIPSC-CĬC,CH (PSP°PìCĤPëPeP»P°Pr, C,CĬP¶PeC-
CĬPμCĤCĬPμPIPs-CĬCĬPrPëPSPSC- CĤPsP·P»P°PrPë, C,P°PeC- CĬPe PSPμCĬC,P°P±C-P»CHBPSP°
CĬC,PμPSPsPeP°CĤPrC-CĬ P°P±Ps CĬPμCĤCĬPμPIP° PSPμPrPsCĬC,P°C,PSC-CĬC,CH

C, CIP¶PePsPiPs CÍC, CíPíPµPSCÍ).

- P°C, CĤP°C, P° P·PsCĤCí PSP° PsPrPSPµ PsPePs PIPSP°CÍP»C-PrPsPe
PSPµP°CĤC, PµCĤC-P°P»CHBPSPsC— PíPµCĤPµPrPSCĤPsC— C-C€PµPjC-C‡PSPsC—
PSPµPICĤPsPíP°C, C-C— P·PsCĤPsPiPs PSPµCĤPIP°, PSPµP·P°P»Pµ¶PSPs PIC-Pr C, PsPiPs,
PíPsPiBĤ™ CIP·P°PSP° C†CÍ PíP°C, PsP»PsPiC-CÍ C-P· PíPsPíPµCĤPµPrPSC-Pj
P·P°CÍC, PsCÍCíPIP°PSPSCÍPj C-PSPiC-P±C-C, PsCĤC-PI PαP”P·5 C‡Pě PSC-.

- PkP°CÍPIPSC-CÍC, CH C, P°PePěC... P·P°C... PIPsCĤCĤPIP°PSCĤ: PíPsCĤCíC€PµPSPSCÍ
C,, CíPSPeC†C-C— PíPµC‡C-PSPePě C, CIP¶PePsPiPs CÍC, CíPíPµPSCÍ,
P°CĤC, PµCĤC-P°P»CHBPSP° PiC-PíPsC, PµPSP·C-CÍ (P°CĤC, PµCĤC-P°P»CHBPSPěPNē C, PěCÍPe
PSPěP¶C‡Pµ 90/50 PjPj CĤC,, CÍC,,), PSPµC%oPsPrP°PIPSPs PíPµCĤPµPSPµCÍPµPSPěPNē
C-PSCÍCíP»CHC, P°P±Ps C-PSC,, P°CĤPeC, PjC-PsPeP°CĤPrP° C, P° CÍPíP°PrPePsPIC-
PrPµPíPµPSPµCĤP°C, PěPIPSC- P·P°C... PIPsCĤCĤPIP°PSPSCÍ CÍC-C, PeC-PIPePě, C, P°PeC- CÍPe
PíC-PíPjPµPSC, PSPěPNē CĤPµC, PěPSC-C, (PSPµPIPµP»PěPeP° PeC-P»CHPeC-CÍC, CH
C, P°PePěC... PíP°C†C-C”PSC, C-PI PjP°C” PíPµPSPµC, PěC‡PSC- CĤPsP·P»P°PrPě
C,, PsCÍC,, PsPrC-PµCÍC, PµCĤP°P· CÍC-C, PeC-PIPePě), BĤ” PsCÍPeC-P»CHPePě P±PµP·PíPµPeP°
CÍPěP»PrPµPSP°C,, C-P»Cí PSPµ PrPsCÍP»C-PrP¶CíPIP°P»P°CÍCÍ Cí CĤP°P·C- C, P°PePěC...
P·P°C... PIPsCĤCĤPIP°PSCĤ.

**P’P·P°C”PjPsPrC-CÍ P· C-PSC€PěPjPě P»C-PeP°CĤCÍCHPePěPjPě P·P°CÍPsP±P°PjPě C, P°
C-PSC€C- PIPěPrPě PIP·P°C”PjPsPrC-PNē.**

P·C,, PµPeC, Pě C-PSC€PěC... P»C-PeP°CĤCÍCHPePěC... P·P°CÍPsP±C-PI PSP°
CÍPěP»PrPµPSP°C,, C-P»

P”PsCÍP»C-PrP¶PµPSPSCÍ in vitro

PĤPµC, P°P±PsP»C-P·Pj CÍPěP»PrPµPSP°C,, C-P»Cí PIC-PrP±CíPIP°C”C, CHCÍCÍ
PíPµCĤPµPIP°P¶PSPs P·P° CíC‡P°CÍC, CĤ C-P·PsC,, PsCĤPjPě 3PĤ4 (PíPsP»PsPIPSPěPNē
C€P»CÍC...) C, P° C-P·PsC,, PsCĤPjPě 2PŸ9 (PrCĤCíPíPsCĤCÍPrPSPěPNē C€P»CÍC...) C†PěC, PsC... CĤPsPjCí P 450 (CYP). PŸPsPjCí C-PSPiC-P±C-C, PsCĤPě C†PěC...
C-P·PsC,, PµCĤPjPµPSC, C-PI PjPsP¶CíC, CH P·PSPěP¶CíPIP°C, Pě PeP»C-CĤPµPSCÍ
CÍPěP»PrPµPSP°C,, C-P»Cí, P° C-PSPrCíPeC, PsCĤPě C†PěC... C-P·PsC,, PµCĤPjPµPSC, C-PI
PjPsP¶CíC, CH PíC-PrPIPěC%oCíPIP°C, Pě PeP»C-CĤPµPSCÍ CÍPěP»PrPµPSP°C,, C-P»Cí.

P”PsCÍP»C-PrP¶PµPSPSCÍ in vivo

PµPsPíCíP»CÍC†C-PNēPSPěPNē C,, P°CĤPjP°PePsPeC-PSPµC, PěC‡PSPěPNē P°PSP°P»C-P·
PrP°PSPěC... PeP»C-PSC-C‡PSPěC... PrPsCÍP»C-PrP¶PµPSCĤ
PíCĤPsPrPµPjPsPSCÍC, CĤCíPIP°PI P·PSPěP¶PµPSPSCÍ PeP»C-CĤPµPSCÍCí
CÍPěP»PrPµPSP°C,, C-P»Cí PíCĤPě PNēPsPiPs PsPrPSPsC‡P°CÍPSPsPjCí
P·P°CÍC, PsCÍCíPIP°PSPSC- P· C-PSPiC-P±C-C, PsCĤP°PjPě CYP3A4 (C, P°PePěPjPě CÍPe
PePµC, PsPePsPSP°P·PsP», PµCĤPěC, CĤPsPjC-C†PěPS, C†PěPjPµC, PěPrPěPS). PÍPsC‡P° PíCĤPě
PsPrPSPsC‡P°CÍPSPsPjCí P·P°CÍC, PsCÍCíPIP°PSPSC- CÍPěP»PrPµPSP°C,, C-P»Cí C, P°
C-PSPiC-P±C-C, PsCĤC-PI CYP3A4 P·CĤPsCÍC, P°PSPSCÍ C‡P°CÍC, PsC, Pě PíPsP±C-C‡PSPěC...
CÍPIPěC%o PSPµ CÍPíPsCÍC, PµCĤC-PíP°P»PsCÍCÍ, CÍP»C-Pr CĤPsP·PíP»CÍPSCíC, Pě
PjPsP¶P»PěPIC-CÍC, CH P·P°CÍC, PsCÍCíPIP°PSPSCÍ PíPsC‡P°C, PePsPiPsC— PrPsP·Pě
CÍPěP»PrPµPSP°C,, C-P»Cí 25 PjPi.

PĤPrPSPsC‡P°CÍPSPµ P·P°CÍC, PsCÍCíPIP°PSPSCÍ C-PSPiC-P±C-C, PsCĤP° P’P†P·-

PiC_HPsC,PμP°P·Pë C_HPëC,PSP°PIC-C_HCr, PrCrP¶Pμ PiPsC,CrP¶PSPsPiPs
C-PSPIc-P±C-C,PSc_HP° P 450, Cr C_FC,P°PSC- C_HC-PIPSPsPIP°P¶PSPsC—
PePsPSC†PμPSC,C_HP°C†C-C— (500 PjPi 2 C_HP°P· PSP° PrPsP±Cr) C,P° C_FPëP»PrPμPSP°C,,C-P»Cr
(PsPrPSPsC_HP°P·PsPIP° PrPsP·P° 100 PjPi) PiC_HPëP·PIPsPrPëP»Ps PrPs PiC-PrPIPëC%PμPSPSC¶
C_{max} C_FPëP»PrPμPSP°C,,C-P»Cr PSP° 300 % (Cr 4 C_HP°P·Pë) C,P° PiC-PrPIPëC%PμPSPSC¶
PiP»P°P·PjPsPIPsC— AUC C_FPëP»PrPμPSP°C,,C-P»Cr PSP° 1000 % (Cr 11 C_HP°P·C-PI).
P§PμC_HPμP· 24 PiPsPrPëPSPë PiP»P°P·PjPsPIC- C_HC-PIPSC- C_FPëP»PrPμPSP°C,,C-P»Cr PIC_FPμ
C%Pμ C_FC,P°PSPsPIPëP»Pë PiC_HPëP±P»PëP·PSPs 200 PSPI/PjP», PiPsC_HC-PIPSC¶PSPs P·
C_HC-PIPSPμPj PiC_HPëP±P»PëP·PSPs 5 PSPI/PjP», C...P°C_HP°PeC,PμC_HPSPëPj PrP»C¶
P·P°C_FC,PSc_FC_FPIP°PSPSC¶ C,C-P»CHPePë C_FPëP»PrPμPSP°C,,C-P»Cr, C%Ps
PIC-PrPiPsPIC-PrP°C” P·PSP°C‡PSPsPjCr PIPiP»PëPIC_F C_HPëC,PSP°PIC-C_HCr PSP°
C€PëC_HPsPePëPNë C_FPiPμPeC,C_H C_FC_FP±C_FC,C_HP°C,C-PI P 450. PÿPëP»PrPμPSP°C,,C-P» PSPμ
PIPiP»PëPIP°C” PSP° C,,P°C_HPjP°PePsPeC-PSPMμC,PëPeCr C_HPëC,PSP°PIC-C_HCr. P—
PsPiP»C¶PrCr PSP° C†C- C,,P°C_HPjP°PePsPeC-PSPMμC,PëC‡PSC- PrP°PSC- PsPrPSPsC‡P°C_FPSMμ
P·P°C_FC,PSc_FC_FPIP°PSPSC¶ C_FPëP»PrPμPSP°C,,C-P»Cr C,P° C_HPëC,PSP°PIC-C_HCr PSPμ
C_HPμPePsPjPμPSPrC_FC”C,CHC_FC¶ (PrPëPI. C_HPsP·PrC-P» B«PhC_FPsP±P»PëIPsC_FC,C-
P·P°C_FC,PSc_FC_FPIP°PSPSC¶B»); Cr PePsP¶PSPsPjCr C_HP°P·C- PjP°PeC_FPëPjP°P»CHPSP°
PrPsP·P° C_FPëP»PrPμPSP°C,,C-P»Cr PSPμ PiPsPIPëPSPSP° PiPμC_HPμPIPëC%CrPIP°C,Pë 25 PjPi
PiC_HPsC,C¶PiPsPj 48 PiPsPrPëPS.

PjPePjPsP»CH, PIPiP»PëPI PíCĤPμPĪP°CĤP°C,Cr PSP° PeP»C-CĤPμPSCÍ CrCrP±CÍC,CĤP°C,C-PI C†PëC... C-P·PsC,,PμCĤPjPμPSC,C-PI PjP°P»PsPNëPjPsPIC-CĤPSPëPNë.

P'C-PrCÍCrC,PSC- PrP°PSC- C%PsPrPs PIP·P°C"PjPsPrC-C— CÍPëP»PrPμPSP°C,,C-P»Cr C- C,P°PePëC... PSPμCÍPīPμC†PëC,,C-C†PSPëC... C-PSPiC-P±C-C,PSCĤC-PI C,,PsCÍC,,PsPrC-PμCÍC,PμCĤP°P·Pë, CĬPe C,PμPsC,,C-P»C-PS C,P° PrPëPiC-CĤPëPrP°PjPsP».

P"PsCÍP»C-PrP¶PμPSPSCĬ in vivo

PhCÍPeC-P»CHPePëB B PIC-PrPsPjPs,B B B C%PsB B CÍPëP»PrPμPSP°C,,C-P»B B PjP°C"B B PIPiP»PëPI B B PSP° B B PjPμC,P°P±PsP»C-P·Pj B NO/C†P"PĥPα, P±CrP»Ps PICÍC,P°PSPsPIP»PμPSPs, C%Ps CÍPëP»PrPμPSP°C,,C-P» PiPsC,PμPSC†C-CĤC" PiC-PiPsC,PμPSP·PëPIPSCr PrC-CĤ PSC-C,CĤP°C,C-PI, C,PSPjCr PNëPsPiPs PsPrPSPsC†P°CÍPSPμ P·P°CÍC,PSCÍCrPIP°PSPSCĬ P· PrPsPSPsCĤP°PjPë PsPeCÍPëPrCr P°P·PsC,Cr P°P±Ps P· PSC-C,CĤP°C,P°PjPë Cr P±CrPrCH-CĬPeC-PNë C,,PsCĤPjC- PíCĤPsC,PëPiPsPeP°P·P°PSPμ (PrPëPI. CĤPsP·PrC-P» B«PμCĤPsC,PëPiPsPeP°P·P°PSPSCĬB»).

P C-PsC†PëPiCâP°C,. P"PsPeP»C-PSC-C†PSC- PrPsCÍP»C-PrP¶PμPSPSCĬ PíCĤPsPrPμPjPsPSCÍC,CĤCrPIP°P»Pë P°PrPëC,PëPIPSPëPNë CÍPëCÍC,PμPjPSPëPNë PμC,,PμPeC, P·PSPëP¶PμPSPSCĬ P°CĤC,PμCĤC-P°P»CHPSPsPiPs C,PëCÍPeCr PíCĤPë PsPrPSPsC†P°CÍPSPsPjCr P·P°CÍC,PSCÍCrPIP°PSPSC- C-PSPiC-P±C-C,PSCĤC-PI PαP"P·5 P· CĤC-PsC†PëPiCrP°C,PSPj. PĥP»C-PSC-C†PSC- PrPsCÍP»C-PrP¶PμPSPSCĬ PíCĤPsPrPμPjPsPSCÍC,CĤCrPIP°P»Pë, C%Ps CĤC-PsC†PëPiCrP°C, PiPsCÍPëP»CĤC" PiC-PiPsC,PμPSP·PëPIPSCr PrC-CĤ C-PSPiC-P±C-C,PSCĤC-PI PαP"P·5.

PJ PīP°C†C-C"PSC,C-PI, CĬPeC- P±CĤP°P»Pë CrC†P°CÍC,CH Cr PrPsCÍP»C-PrP¶PμPSPSC-, PSPμ CÍPiPsCÍC,PμCĤC-PiP°P»PsCÍCH PiPsP·PëC,PëPIPSPsPiPs PeP»C-PSC-C†PSPsPiPs PμC,,PμPeC,Cr PIC-Pr PsPrPSPsC†P°CÍPSPsPiPs P·P°CÍC,PSCÍCrPIP°PSPSCĬ C-PSPiC-P±C-C,PSCĤC-PI PαP"P·5 P· CĤC-PsC†PëPiCrP°C,PSPj. PμCĤPsC,PëPiPsPeP°P·P°PSPμ PsPrPSPsC†P°CÍPSPμ P·P°CÍC,PSCÍCrPIP°PSPSCĬ CĤC-PsC†PëPiCrP°C,Cr P· C-PSPiC-P±C-C,PSCĤP°PjPë PαP"P·5 (Cr C,PSPjCr C†PëCÍP»C- P·C- CÍPëP»PrPμPSP°C,,C-P»PsPj) (PrPëPI. CĤPsP·PrC-P»B B«PμCĤPsC,PëPiPsPeP°P·P°PSPSCĬB»).

PhPrPSPsC†P°CÍPSPμ P·P°CÍC,PSCÍCrPIP°PSPSCĬ CÍPëP»PrPμPSP°C,,C-P»Cr C,P° P±P»PsPeP°C,PSCĤC-PI α-P°PrCĤPμPSPsCĤPμC†PμPiC,PSCĤC-PI PjPsP¶Pμ PíCĤPëP·PIPμCÍC,Pë PrPs CĤPsP·PIPëC,PeCr CÍPëPjPiC,PSPjP°C,PëC†PSPsC— PiC-PiPsC,PμPSP·C-C— Cr PrPμCĬPePëC... CÍC...PëP»CHPSPëC... PrPs C†CHPsPiPs PīP°C†C-C"PSC,C-PI. PŷP°PeP° CĤPμP°PeC†C-CĬ PSP°PNëC†P°CÍC,C-C€Pμ PIPëPSPëPeP°P»P° PíCĤPsC,CĬPiPsPj 4 PiPsPrPëPS PíC-CÍP»CĬ P·P°CÍC,PSCÍCrPIP°PSPSCĬ CÍPëP»PrPμPSP°C,,C-P»Cr (PrPëPI. CĤPsP·PrC-P»Pë B«PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PSCÍCrPIP°PSPSCĬB» C,P° B«PŷPiPsCÍC-P± P·P°CÍC,PSCÍCrPIP°PSPSCĬ C,P° PrPsP·PëB»). PJ PíCĤPsC†PμCÍC- 3 PrPsCÍP»C-PrP¶PμPSCĤ CÍPiPμC†PëC,,C-C†PSPsC— PIP·P°C"PjPsPrC-C— P»C-PeP°CĤCÍCHPePëC... P·P°CÍPsP±C-PI P±P»PsPeP°C,PSCĤ α-P°PrCĤPμPSPsCĤPμC†PμPiC,PSCĤC-PI PrPsPeCÍP°P·PsP·PëPS (4 PjPi C,P° 8 PjPi) C,P° CÍPëP»PrPμPSP°C,,C-P» (25 PjPi, 50 PjPi C,P° 100 PjPi) P·P°CÍC,PSCÍPsPICrPIP°P»Pë PsPrPSPsC†P°CÍPSPs PīP°C†C-C"PSC,P°Pj C-P· PrPsP±CĤPsCĬPeC-CÍPSPsCĤ PiC-PiPμCĤPīP»P°P·C-C"CĤ PīPμCĤPμPrPjC-C...CrCĤPsPiPsC— P·P°P»PsP·Pë, CÍC,P°P±C-P»C-P·P°C†C-CĬ CÍC,P°PSCr CĬPePëC... P±CrP»P° PrPsCÍCĬPiPSCrC,P° PíCĤPë P·P°CÍC,PSCÍCrPIP°PSPSC- PrPsPeCÍP°P·PsP·PëPSCr. PJ C†PëC... PiPsPiCrP»CĬC†C-CĬC... CÍPiPsCÍC,PμCĤC-PiP°P»PsCÍCĬ CÍPμCĤPμPrPSC" PrPsPrP°C,PePsPiPμ P·PSPëP¶PμPSPSCĬ P°CĤC,PμCĤC-P°P»CHPSPsPiPs C,PëCÍPeCr Cr PiPsP»PsP¶PμPSPSC- P»PμP¶P°C†Pë PSP° 7/7 PjPj CĤC,. CÍC,.. 9/5 PjPj CĤC,. CÍC,. C,P° 8/4 PjPj CĤC,. CÍC,. C,P° CÍPμCĤPμPrPSC" P·PSPëP¶PμPSPSCĬ P°CĤC,PμCĤC-P°P»CHPSPsPiPs C,PëCÍPeCr Cr PiPsP»PsP¶PμPSPSC-

СГГ,PsCЦC±Pë PSP° 6/6 PjPj CГC,, СГГ,, 11/4 PjPj CГC,, СГГ,, 4/5 PjPj CГC,, СГГ,,
PIC-PrPіPsPIC-PrPSPs. PμCГPë PsPrPSPsC±P°CГPSPsPjCр P·P°CГC,PsCГCрPIP°PSPSC-
CГPëP»PrPμPSP°C,,C-P»Cр C,P° PrPsPeCГP°P·PsP·PëPSCр PіP°CГC-C”PSC,P°Pj,
CГC,P°P±C-P»C-P·P°CГC-CЦ CГC,P°PSCр CЦPePëC... P±CрP»P° PrPsCГCЦPіPSCрC,P° PіCГPë
P·P°CГC,PsCГCрPIP°PSPSC- PrPsPeCГP°P·PsP·PëPSCр, C-PSPsPrC-
PіPsPIC-PrPsPjP»CЦP»PsCГCЦ PіCГPs CГPsP·PIPëC,PsPe CГPëPjPіC,PsPjP°C,PëC±PSPsC—
PsCГC,PsCГC,P°C,PëC±PSPsC— PіC-PіPsC,PμPSP·C-C—. PJ CГPëC...
PіPsPIC-PrPsPjP»PμPSPSCЦC... P№CєP»PsCГCЦ PіCГPs PIPëPіP°PrPePë
P·P°PіP°PjPsCГPsC±PμPSPSCЦ C,P° CГC,P°PS PіPμCГPμPr PSPμPіCГPëC,PsPjPSC-CГC,CГ,
P°P»Pμ P±PμP· CГPëPSPePsPіPμ.

PкPμ CГPіPsCГC,PμCГC-PіP°P»PsCГCЦ P¶PsPrPSPëC... P·PSP°C±CрC%PëC...
PIP·P°C”PjPsPrC-P№ PіCГPë PsPrPSPsC±P°CГPSPsPjCр P·P°CГC,PsCГCрPIP°PSPSC-
CГPëP»PrPμPSP°C,,C-P»Cр (50 PjPi) C- C,PsP»P±CрC,P°PjC-PrCр (250 PjPi) P°P±Ps
PIP°CГC,,P°CГPëPSCр (40 PjPi), C%Ps PjPμC,P°P±PsP»C-P·CрCГC,CГCГCЦ CYP2C9.

PŸPëP»PrPμPSP°C,,C-P» (50 PjPi) PSPμ PіCГPëP·PIPsPrPëPI PrPs PіPsPrPsPIP¶PμPSPSCЦ
C±P°CГCр PeCГPsPIPsC,PμC±C-, CГPіCГPëC±PëPSPμPSPsC— P·P°CГC,PsCГCрPIP°PSPSCЦPj
P°CГPμC,PëP»CГP°P»C-CГPëP»PsPIPsC— PePëCГP»PsC,Pë (150 PjPi).

PŸPëP»PrPμPSP°C,,C-P» (50 PjPi) PSPμ PіPsC,PμPSCГC-CГPIP°PI PіC-PіPsC,PμPSP·PëPIPsCр
PrC-CГ P°P»PePsPіPsP»CГ Cр P·PrPsCГPsPIPëC... PrPsP±CГPsPIPsP»CГCГC-PI PіCГPë
CГPμCГPμPrPSCГPsPjCр PjP°PeCГPëPjP°P»CГPSPsPjCр CГC-PIPsC- PμC,P°PSPsP»Cр
PeCГPsPIC- 80 PjPi/PrP».

PJ PіP°CГC-C”PSC,C-PI, CЦPeC- P·P°CГC,PsCГPsPICрPIP°P»Pë CГPëP»PrPμPSP°C,,C-P», PSPμ
CГPіPsCГC,PμCГC-PіP°P»PsCГCЦ P¶PsPrPSPëC... PIC-PrPjC-PSPSPsCГC,PμP№ PіCГPsC,,C-P»CГ
PіPsP±C-C±PSPëC... PμC,,PμPeC,C-PI PіPsCГC-PIPsCЦPSPs P· PіP»P°CГPμP±Ps PіCГPë
PsPrPSPsC±P°CГPSPsPjCр P·P°CГC,PsCГCрPIP°PSPSC- C,P°PePëC... PeP»P°CГC-PI
PіC-PіPsC,PμPSP·PëPIPsPëC... P»C-PeP°CГCГCГPePëC... P·P°CГPsP±C-PI, CЦPe
PrC-CрCГPμC,PëPePë, P±P»PsPeP°C,PsCГPë β-P°PrCГPμPSPsCГPμCГPμPіC,PsCГC-PI,
C-PSPіC-P±C-C,PsCГPë PђPұPα, P°PSC,P°PіPsPSC-CГC,Pë P°PSPіC-PsC,PμPSP·PëPSCр PГPГ,
P°PSC,PëPіC-PіPμCГC,PμPSP·PëPIPsC- P»C-PeP°CГCГCГPeC- P·P°CГPsP±Pë
(CГCрPrPëPSPsCГPsP·CєPëCГCГPIP°P»CГPSC- C,P° CГPμPSC,CГP°P»CГPSPsC— PrC-C—),
P±P»PsPeP°C,PsCГPë P°PrCГPμPSPμCГPіC-C±PSPëC... PSPμP№CГPsPSC-PI,
P±P»PsPeP°C,PsCГPë PeP°P»CГCГC-C”PIPëC... PeP°PSP°P»C-PI C,P° P±P»PsPeP°C,PsCГPë α-
P°PrCГPμPSPsCГPμCГPμPіC,PsCГC-PI.

PJ CГPіPμCГC-P°P»CГPSPsPjCр PrPsCГP»C-PrP¶PμPSPSC- PIP·P°C”PjPsPrC-C— PіCГPë
PsPrPSPsC±P°CГPSPsPjCр P·P°CГC,PsCГCрPIP°PSPSC- CГPëP»PrPμPSP°C,,C-P»Cр (100 PjPi) C,P°
P°PjP»PsPrPëPіC-PSCр PіP°CГC-C”PSC,P°Pj C-P· P°CГC,PμCГC-P°P»CГPSPsCГ
PіC-PіPμCГC,PμPSP·C-C”CГ CГPіPsCГC,PμCГC-PіP°P»PsCГCЦ PrPsPrP°C,PePsPIPμ
P·PSPëP¶PμPSPSCЦ CГPëCГC,PsP»C-C±PSPsPіPs P°CГC,PμCГC-P°P»CГPSPsPіPs C,PëCГPeCр PI
PіPsP»PsP¶PμPSPSC- P»PμP¶P°C±Pë PSP° 8 PjPj CГC,, CГC,. P’C-PrPіPsPIC-PrPSPμ
P·PSPëP¶PμPSPSCЦ PrC-P°CГC,PsP»C-C±PSPsPіPs P°CГC,PμCГC-P°P»CГPSPsPіPs C,PëCГPeCр
CГC,P°PSPsPIPëP»Ps 7 PjPj CГC,, CГC,. PіC- PrPsPrP°C,PePsPIC- P·PSPëP¶PμPSPSCЦ
P°CГC,PμCГC-P°P»CГPSPsPіPs C,PëCГPeCр P±CрP»Pë PіPsCГC-PIPsCЦPSPSPëPjPë P·
C,P°PePëPjPë, C%Ps CГPіPsCГC,PμCГC-PіP°P»PëCГCЦ PіCГPë P·P°CГC,PsCГCрPIP°PSPSC-
P»PëCєPμ CГPëP»PrPμPSP°C,,C-P»Cр Cр P·PrPsCГPsPIPëC... PrPsP±CГPsPIPsP»CГCГC-PI.

PŸPëP»PrPμPSP°C,,C-P» Cр PrPsP·C- 100 PjPi PSPμ PIPіP»PëPIP°PI PSP°
C,,P°CГPjP°PePsPeC-PSPμC,PëC±PSC- PіPsPeP°P·PSPëPePë C-PSPіC-P±C-C,PsCГC-PI P’PГP>-

PhCfPec-P»CHPePë CfPµPeCfCfP°P»CHPSP° P°PeC,PëPIPSC-CfC,CH
CfCfPîCtjPsPIPsPrP¶CfC”C,CHCfCµ PîPµPIPSPëPj CtjPëP·PëPePsPj P· P±PsPeCf CfPµCtjC†Cµ,
PrPs PîPsC†P°C,PeCf P±CfPrCH-CµPePsPiPs P»C-PeCfPIP°PSPSCµ PµCtjPµPeC,PëP»CHPSPsC—
PrPëCfC,,CfPSPeC†C— P»C-PeP°Ctj PjP°C” PsC†C-PSPëC,Pë CfC,P°PS CfPµCtjC†PµPIPs-
CfCfPrPëPSPSPsC— CfPëCfC,PµPjPë PîP°C†C-C”PSC,P°. PÿPëP»PrPµPSP°C,,C-P»
C†PëPSPëC,CH CfCfPrPëPSPsCtjPsP·CëPëCtjCtjPIP°P»CHPSCf PrC-Ct, C%Ps
PîCtjPsCµPIP»CµC”C,CHCfCµ P»PµPiPePëPj C,P° PePsCtjPsC,PePsC†P°CfPSPëPj
P·PSPëP¶PµPSPSCµPj P°CtjC,PµCtjC-P°P»CHPSPsPiPs C,PëCfPeCf. P”Ps
PîCtjPëP·PSP°C†PµPSPSCµ CfPëP»PrPµPSP°C,,C-P»Cf P»C-PeP°Ctj PjP°C” CtjPµC,PµP»CHPSPs
P·PIP°P¶PëC,Pë, C†Pë PjPsP¶Pµ C,P°PePëPµ PµC,,PµPeC, PSPµCfPîCtjPëCµC,P»PëPIPs
PIPîP»PëPIP°C,Pë PSP° PîP°C†C-C”PSC,C-PI C-P· PîPµPIPSPëPjPë PsCfPSPsPIPSPëPjPë
P·P°C...PIPsCtjCtjPIP°PSPSCµPjPë, PsCfPsP±P»PëPIPs Cf PePsPjP±C-PSP°C†C— C-P·
CfPµPeCfCfP°P»CHPSPsCt P°PeC,PëPIPSC-CfC,Ct. P”Ps PîP°C†C-C”PSC,C-PI C-P·
PîC-PrPIPëC%PµPSPsCt C†CfC,P»PëPIC-CfC,Ct PrPs PIP°P·PsPrPëP»CµC,P°C,PsCtjC-PI
PSP°P»PµP¶P°C,CH PîP°C†C-C”PSC,Pë C-P· PsP±CfC,CtjCfPeC†C-C”Ct PIPëPIC-PrPSPsPiPs
C,CtjP°PeC,Cf P»C-PIPsPiPs CëP»CfPSPsC†PeP° (PSP°PîCtjPëPeP»P°Pr, CfC,PµPSPsP·
P°PsCtjC,Pë, PîC-PîPµCtjC,CtjPsC,,C-C†PSP° PsP±CfC,CtjCfPeC,PëPIPSP°
PeP°CtjPrC-PsPjC-PsPîP°C,C-Cµ) C,P° PîP°C†C-C”PSC,Pë C-P· CtjC-PrPeC-CfPSPëPj
CfPëPSPrCtjPsPjPsPj PjCfP»CHC,PëCfPëCfC,PµPjPSPsC— P°C,CtjPsC,,C-C—, PsPrPSPëPj C-P·

$P_hPrPSPsC\ddagger P^\circ C\acute{I}PSP\mu P\cdot P^\circ C\acute{I}C,PsC\acute{I}C\acute{I}PIP^\circ PSPSC\acute{I} P\cdot C-PSC\epsilon P\ddot{e}PjP\ddot{e} C-PSPiC-P\pm C-C,PsC\grave{H}P^\circ PjP\ddot{e}$
 $P\alpha P^\circ P\cdot 5 P^\circ P\pm Ps C-PSC\epsilon P\ddot{e}PjP\ddot{e} PiC\grave{H}P\mu PiP^\circ C\grave{H}P^\circ C,P^\circ PjP\ddot{e} PrP\rangle C\acute{I} P\rangle C-P\epsilon C\acute{I}PIP^\circ PSPSC\acute{I}$
 $P\mu C\grave{H}P\mu PeC,P\ddot{e}P\rangle CH\ddot{P}SPsC- PrP\ddot{e}C\acute{I}C,,C\acute{I}PSP\epsilon C\ddagger C-C-$

P'PμP·PīPμPeP° C,P° PμC,,PμPeC,PēPIPSC-Cl'C,CH PsPrPSPsC‡P°Cl'PSPsPiPs
P·P°Cl'C,PsCl'CfPIP°PSPSClI Cl'PēP»PrPμPSP°C,,C-P»Cr P· C-PSC€PēPjPē
C-PSPIc-P±C-C,PsCḡP°PjPē PαP''P•5 P°P±Ps C-PSC€PēPjPē PīCḡPμPīP°CḡP°C,P°PjPē PrP»ClI
P»C-PeCfPIP°PSPSClI PiC-PīPμCḡC,PμPSP·C-C— P»PμPīPμPSPμPIPsC— P°CḡC,PμCḡC-C—,
ClIPeC- PjC-Cl'C,ClIc,CH Cl'PēP»PrPμPSP°C,,C-P», C‡Pē P· C-PSC€PēPjPē
PīCḡPμPīP°CḡP°C,P°PjPē PrP»ClI P»C-PeCfPIP°PSPSClI PμCḡPμPeC,PēP»CHPSPsC—
PrPēCl'C,,CfPSPeC‡C-C— PSPμ PIPēPIC‡P°P»PēCl'ClI. PŷPsPjCf P·P°Cl'C,PsCl'CfPIP°PSPSClI
C,P°PePēC... PePsPjP±C-PSP°C‡C-PNē PSPμ CḡPμPePsPjPμPSPPrPsPIP°PSPμ.

P'PīP»PēPI PSP° P·C-Cḡ

PμPsPIC-PrPsPjP»ClI»PsCl'CH PīCḡPs PIPēPSPēPePSPμPSPSClI PrPμC,,PμPeC,C-PI P·PsCḡCf
C,P° PIPēPīP°PrPePē PSPμP°CḡC,PμCḡC-P°P»CHPSPsC— PīPμCḡPμPrPSCḡPsC—
C-C€PμPjC-C‡PSPsC— PSPμPICḡPsPīP°C,C-C— P·PsCḡPsPIPsPiPs PSPμCḡPIP° Cf
P·PIBḡ™ ClI·PeCf C-P· P·P°Cl'C,PsCl'CfPIP°PSPSClI Pj Cl'PēP»PrPμPSP°C,,C-P»Cr C,P°
C-PSC€PēC... C-PSPIc-P±C-C,PsCḡC-PI PαP''P•5 (PrPēPI. CḡPsP·PrC-P» B«PμPsP±C-C‡PSC-
CḡPμP°PeC‡C-C—B»). PμP°C‡C-C''PSC,C-PI Cl'P»C-Pr PīPsPīPμCḡPμPrPēC,Pē, C‰Ps Cf
CḡP°P·C- CḡP°PīC,PsPIPsPiPs PīPsCḡCfC€PμPSPSClI P·PsCḡCf P·P°Cl'C,PsCl'CfPIP°PSPSClI
PīCḡPμPīP°CḡP°C,Cf Cl'P»C-Pr PīCḡPēPīPēPSPēC,Pē C,P° PSPμPīP°PNēPSPs
P·PIPμCḡPSCfC,PēCl'ClI PrPs P»C-PeP°CḡClI (PrPēPI. CḡPsP·PrC-P»
B«PμCḡPsC,PēPīPsPeP°P·P°PSPSClI»).

PḡPrPSPsC‡P°Cl'PSPμ P·P°Cl'C,PsCl'CfPIP°PSPSClI P· CḡPēC,PsPSP°PIC-CḡPsPj

PḡPrPSPsC‡P°Cl'PSPμ P·P°Cl'C,PsCl'CfPIP°PSPSClI Cl'PēP»PrPμPSP°C,,C-P»Cr C,P°
CḡPēC,PsPSP°PIC-CḡCf PSPμ CḡPμPePsPjPμPSPPrCfC''C,CHCl'ClI (PrPēPI. CḡPsP·PrC-P»
B«P'P·P°C''PjPsPrC-ClI P· C-PSC€PēPjPē P»C-PeP°CḡCl'CHPePēPjPē P·P°Cl'PsP±P°PjPē C,P°
C-PSC€C- PIPēPrPē PIP·P°C''PjPsPrC-PNēB»).

*PḡPrPSPsC‡P°Cl'PSPμ P·P°Cl'C,PsCl'CfPIP°PSPSClI P· P±P»PsPeP°C,PsCḡP°PjPē α-
P°PrCḡPμPSPsCḡPμC‡PμPīC,PsCḡC-PI*

PμP°C‡C-C''PSC,P°Pj, ClIPeC- P·P°Cl'C,PsCl'PsPICfCḡC,CH P±P»PsPeP°C,PsCḡPē α-
P°PrCḡPμPSPsCḡPμC‡PμPīC,PsCḡC-PI, P·P°Cl'C,PsCl'PsPICfPIP°C,Pē Cl'PēP»PrPμPSP°C,,C-P»
Cl'P»C-Pr P· PsP±PμCḡPμP¶PSC-Cl'C,CH, PsCl'PeC-P»CHPePē C,P°PeP° PePsPjP±C-PSP°C‡C-ClI
PjPsP¶Pμ PīCḡPēP·PIPμCl'C,Pē PrPs Cl'PēPjPīC,PsPjP°C,PēC‡PSPsC— PiC-PīPsC,PμPSP·C-C— Cf
PrPμClIPePēC... Cl'C...PēP»CHPSPēC... PrPs C‡CHPsPiPs PīP°C‡C-C''PSC,C-PI.
PŷPēPjPīC,PsPjP°C,PēC‡PSP° PiC-PīPsC,PμPSP·C-ClI P·P°P·PIPēC‡P°PNē PIPēPSPēPeP°C''
PīCḡPsC,ClIPiPsPj 4 PiPsPrPēPS PīC-Cl'P»ClI P·P°Cl'C,PsCl'CfPIP°PSPSClI
Cl'PēP»PrPμPSP°C,,C-P»Cr. PŷPsPjCf PrPs PīPsC‡P°C,PeCf P·P°Cl'C,PsCl'CfPIP°PSPSClI
Cl'PēP»PrPμPSP°C,,C-P»Cr PiPμPjPsPrPēPSP°PjC-C‡PSC- PīPsPeP°P·PSPēPePē PīP°C‡C-C''PSC,P°
PīCḡPē C,PμCḡP°PīC-C— P±P»PsPeP°C,PsCḡP°PjPē α-P°PrCḡPμPSPsCḡPμC‡PμPīC,PsCḡC-PI
PjP°CḡC,CH P±CfC,Pē Cl'C,P°P±C-P»CHPSPēPjPē. PŷP»C-Pr CḡPsP·PīP»ClIPSCfC,Pē
PjPsP¶P»PēPIC-Cl'C,CH P·P°Cl'C,PsCl'CfPIP°PSPSClI PīPsC‡P°C,PePsPIPsC— PrPsP·Pē
Cl'PēP»PrPμPSP°C,,C-P»Cr 25 PjPi (PrPēPI. CḡPsP·PrC-P» B«PŷPīPsCl'C-P±
P·P°Cl'C,PsCl'CfPIP°PSPSClI C,P° PrPsP·PēB»). PḡCḡC-Pj C,PsPiPs, PīPsC,CḡC-P±PSPs
PīCḡPsC-PSC,,PsCḡPjCfPIP°C,Pē PīP°C‡C-C''PSC,C-PI, ClIPe PrC-ClIc,Pē Cf CḡP°P·C-
PīPsClIPIPē Cl'PēPjPīC,PsPjC-PI PsCḡC,PsCl'C,P°C,PēC‡PSPsC— PiC-PīPsC,PμPSP·C-C—.

P'PīP»PēPI PSP° PeCḡPsPIPsC,PμC‡Cž

P''PsCl'P»C-PrP¶PμPSPSClIB B C,CḡPsPjP±PsC‡PēC,C-PI B P»CHPrPēPSPē

В РіСґPsPrPμPjPsPSCГC,СґCрPIP°P»Pё, В C%Ps В in B vitro В CГPёP»PrPμPSP°C,„C-P»B
В PіPsC,РμPSCГC-СґC” P°PSC,PёP°PiCґPμPiP°CГC-PMSC- РμC,„РμPеC,Pё PSP°C,СґC-Сґ
PSC-C,СґPsPiCґCрCГPёPrCр. PкPμPjP°C” P¶PsPrPSPsC— C-PSC,„PsCґPjP°CГC-C— C%PsPrPs
P±PμP·PiPμPеPё P·P°CГC,PsCГCрPIP°PSPSCГ CГPёP»PrPμPSP°C,„C-P»Cр PiP°CГC-C”PSC,P°Pj
C-P· PiPsCґCрCєPμPSPSCГPjPё P·PiPsCґC,P°PSPSCГ PeCґPsPIC- P°P±Ps PiPsCГC,СґPsCґ
PiPμPiC,PёC±PSPsCґ PIPёCґP°P·PePsCґ. PґP°PePёPj C±PёPSPsPj, P·P°CГC,PsCГCрPIP°PSPSCГ
CГPёP»PrPμPSP°C,„C-P»Cр PiP°CГC-C”PSC,P°Pj CГC-C”C— PiCґCрPiPё PjPsP¶P»PёPIPμ
P»PёCєPμ PiC-CГP»CГ CґPμC,РμP»СґPSPsC— PsCГC-PSPePё CГPiC-PIPIC-PrPSPsCєPμPSPSCГ
PePsCґPёCГC,C- C,P° CґPёP·PёPeC-PI.

P’C,CґP°C,P° CГP»CзC...Cз

P>C-PeP°CґCГPj CГP»C-Pr PiPsCґP°PrPёC,Pё PiP°CГC-C”PSC,P°Pj PiCґPёPiPёPSPёC,Pё
P·P°CГC,PsCГCрPIP°PSPSCГ C-PSPiC-P±C-C,PsCґC-PI PαP”P•5, PIPeP»CґC±P°CґC±Pё
PiCґPμPiP°CґP°C, P’C-PIP°PMSCґP°, C,P° PSPμPiP°PMSPs P·PIPμCґPSCрC,PёCГCГ P·P°
PjPμPrPёC±PSPsCґ PrPsPiPsPjPsPiPsCґ Cр CґP°P·C- CґP°PiC,PsPIPsPiPs P·PSPёP¶PμPSPSCГ
C±Pё PIC,CґP°C,Pё CГP»CрC...Cр. PμCґPs CГC- CГPIPёC%P°, CГPeC- C,P°PePsP¶
PjPsP¶CрC,Сґ CГCрPiCґPsPIPsPrP¶CрPIP°C,PёCГCГ PrP·PIPsPSPsPj Cр PICрC...P°C... C,P°
P·P°PiP°PjPsCґPsC±PμPSPSCГPj, PiPsPIC-PrPsPjP»CГP»PsCГCГ P· P°CГPsCГC-P°CГC-C”Cґ Cр
C±P°CГC- C-P· P·P°CГC,PsCГCрPIP°PSPSCГPj C-PSPiC-P±C-C,PsCґC-PI PαP”P•5,
PIPeP»CґC±P°CґC±Pё PiCґPμPiP°CґP°C, P’C-PIP°PMSCґP°. P’PёP·PSP°C±PёC,Pё, C±Pё CГC-
CГPIPёC%P° PiCґCГPjPs PiPsPiCґ™ CГP·P°PSC- C-P· P·P°CГC,PsCГCрPIP°PSPSCГPj
C-PSPiC-P±C-C,PsCґC-PI PαP”P•5, C±Pё P· C-PSCєPёPjPё C,„P°PeC,PsCґP°PjPё,
PSPμPjPsP¶P»PёPIPs.

*PґPrPSPsC±P°CГPSPμ P·P°CГC,PsCГCзPIP°PSPSCГ C-P· PiC-PiPsC,РμPSP·PёPIPSPёPjPё
PiCґPμPiP°CґP°C,P°PjPё*

P’C-PIP°PMSCґP° C±PёPSPёC,Сґ CГPёCГC,РμPjPSCр
CГCрPrPёPSPsCґPsP·CєPёCґCґPIP°P»СґPSCр PrC-Сґ C,P° PjPsP¶Pμ PrP°P»C-
P·PSPёP¶CрPIP°C,Pё P°CґC,РμCґC-P°P»СґPSPёPMSC,PeCГPe Cр PiP°CГC-C”PSC,C-PI, CГPeC-
P·P°CГC,PsCГPsPICрCґC,Сґ PiC-PiPsC,РμPSP·PёPIPSC- P>C-PeP°CґCГCґPeC- P·P°CГPsP±Pё.
Pj PsPeCґPμPjPsPjCр PrPsCГP»C-PrP¶PμPSPSC- P>C-PeP°CґCГCґPePsC— PIP·P°C”PjPsPrC-C—
PiCґPё PsPrPSPsC±P°CГPSPsPjCр P·P°CГC,PsCГCрPIP°PSPSC- P°PjP»PsPrPёPiC-PSCр (5 PjPi
P°P±Ps 10 PjPi) C,P° PiCґPμPiP°CґP°C,Cр P’C-PIP°PMSCґP° (100 PjPi) PiPμCґPsCґP°P»СґPSPs
CГPiPsCГC,РμCґC-PiP°P»PsCГCГ CГPμCґPμPrPSC” PrPsPrP°C,PePsPIPμ P·PSPёP¶PμPSPSCГ
CГPёCГC,PsP»C-C±PSPsPiPs C,PёCГPeCр PSP° 8 PjPj CґC,., CГC,., PrC-P°CГC,PsP»C-C±PSPsPiPs
Bґ” PSP° 7 PjPj CґC,., CГC,.

*P—P°C...PIPсCґCґPIP°PSPSCГ, C%Ps PiPμCґPμPrP°CґC,СґCГCГ CГC,P°C,РμPIPёPj
CєP»CГC...PsPj*

P—P°CГC,PsCГCрPIP°PSPSCГ PiCґPμPiP°CґP°C,Cр P’C-PIP°PMSCґP° PSPμ P·P°C...PёC%P°C”
PIC-Pr P·P°C...PIPsCґCґPIP°PSCґ, C%Ps PiPμCґPμPrP°CґC,СґCГCГ CГC,P°C,РμPIPёPj
CєP»CГC...PsPj. PґP»C-Pr PiCґPsC-PSCГC,СґCрPeC,CрPIP°C,Pё PiP°CГC-C”PSC,C-PI C%PsPrPs
PSPμPsP±C...C-PrPSPёC... P·P°PiPsP±C-P¶PSPёC... P·P°CГPsP±C-PI PrP»CГ P·P°C...PёCГC,Cр
PIC-Pr P·P°C...PIPsCґCґPIP°PSCґ, C%Ps PiPμCґPμPrP°CґC,СґCГCГ CГC,P°C,РμPIPёPj
CєP»CГC...PsPj, PIPeP»CґC±P°CґC±Pё PIC-CґCрCГ C-PjCрPSPsPrPμC,„C-C±PёC,Cр
P»CґPrPёPSPё.

PαPμCґC,PёP»СґPSC-CГC,Сґ

РѹС-СІР»СІ Р·Р°СІС,РсСІСІРІР°РSPSCІ РrPsP·Рё 100 РjРi Р·РrPsСђРsРІРёРjРё
РrPsP±СђРsРІРsР»СђСІСІРjРё РSPµ СІРiРsСІС,РµСђС-РiР°Р»РsСІСІ РІРiР»РёРІСІ РSP°
РjPsСђС,РsР»РsРiС-Сђ СІРё СђСІС...РsРjС-СІС,Сђ СІРiРµСђРjР°С,РsР·РsС—РrС-РІ.

Р"Рs СІРёР»Р°РrСІ Р'С-РІР°РNСђСђР° РІС...РsРrРёС,Сђ Р»Р°РёС,РsР·Р°, СІРёС%Рs СІ Р'Р°СІ
РІСІС,Р°РSPsРІР»РµРSPs РSPµРiРµСђРµРSPsСІРёРjС-СІС,Сђ РrРµСІРёРёС... СІСІРёСђС-РІ,
РiСђРsРёРsРSCІСІР»СђС,СІРNС,РµСІСІ Р· Р»С-РёР°СђРµРj, РiРµСђСё РSC-Р¶
РiСђРёРNСРjР°С,Рё СІРµРNС Р»С-РёР°СђСІСђРёРёРNС Р·Р°СІС-Р±. РђСІРiР°СђС,Р°Рj (Р· 951)
РІ СІРёР»Р°РrС- Р»С-РёР°СђСІСђРёРsРiРs Р·Р°СІСРs±СІ С" РiРsС...С-РrРSPёРj
С,,РµРSC-Р»Р°Р»Р°РSC-РSCІ, С%Рs СІРІР»СІС" РSPµР±РµР·РiРµСІ РrР»СІ
С...РІPsСђРёС... РSP° С,,РµРSC-Р»РёРµС,РsРSCІСђС-Сђ.

*Р—Р°СІС,РsСІСІРІР°РSPSCІ СІ РiРµСђС-РsРr РІР°РiС-С,РSPsСІС,С- Р°Р±Рs
РiРsРrСІРІР°РSPSCІ РiСђСІРrСђ.*

РѹСђРµРiР°СђР°С, РSPµ РiСђРёР·РSP°СІРµРSPёРNС РrР»СІ Р·Р°СІС,РсСІСІРІР°РSPSCІ
Р¶С-РSPёР°РjРё.

*Р—РrР°С,РSC-СІС,Сђ РІРiР»РёРiР°С,Рё РSP° СёРІРёРrРёС-СІС,Сђ СђРµР°РёСІС— РiСђРё
РёРµСђСІРІР°РSPSC- Р°РІС,РsС,СђР°РSCІРiРsСђС,РsРj Р°Р±Рs С-РSCёРёРjРё
РjРµС...Р°РSC-Р·РjР°РjРё.*

Р"РsСІР»С-РrР¶РµРSCђ РІРiР»РёРiР°С РiСђРµРiР°СІ РiСђРµРiР°СђР°С,СІ РSP° Р·РrР°С,РSC-СІС,Сђ
РёРµСђСІРІР°С,Рё С,СђР°РSCІРiРsСђС,РSPёРjРё Р·Р°СІСРs±Р°РjРё С,Р° РiСђР°СІСђРІР°С,Рё
Р· С-РSCёРёРjРё РjРµС...Р°РSC-Р·РjР°РjРё РSPµ РiСђРsРІPsРrРёР»РsСІСІ.

РђСІРёС-Р»СђРёРё СІ РiСђРsСІРµСІС- РёР»С-РSC-СІРSPёС... РrPsСІР»С-РrР¶РµРSCђ
Р·Р°СІС,РсСІСІРІР°РSPSCІ СІРёР»Р»РrРµРSP°С,,С-Р»СІ РiРsРІС-РrPsРjР»СІР»РsСІСІ РiСђРs
РІРёРiР°РrРёРё Р·Р°РiР°РjРsСђСІРµРSPSCІ С,Р° РiРsСђСІСёРµРµРSPSCІ Р· Р±РsРёСІ
РsСђРiР°РSC-РІ Р·РsСђСІ, РiРµСђРµРr С,РёРj, СІРё СІС-РrР°С,Рё Р·Р° РёРµСђРjРs
С,СђР°РSCІРiРsСђС,РSPsРiРs Р·Р°СІСРs±СІ Р°Р±Рs РiСђР°СІСђРІР°С,Рё Р·
РjРµС...Р°РSC-Р·РjР°РjРё, РiР°СІС-С"РSC,Р°Рj РSPµРsР±С...С-РrРSPs Р·Бђ™СІСІСІРІР°С,Рё,
СІРёРsСђ С" С—С...РSCІ С-РSPrРёРІС-РrСІР°Р»СђРSP° СђРµР°РёСІС-СІ РSP°
Р·Р°СІС,РсСІСІРІР°РSPSCІ РiСђРµРiР°СђР°С,СІ.

РŸРiРsСІС-Р± Р·Р°СІС,РсСІСІРІР°РSPSCІ С,Р° РrPsP·Рё.

РѹСђРµРiР°СђР°С, Р·Р°СІС,РсСІРsРІСІСђС,Сђ РiРµСђРsСђР°Р»СђРSPs.

РŸР°Р±Р»РµСІ СІР»С-Рr РiРsРІРSC-СІС,Сђ СђРsР·Р¶СІРІР°С,Рё С,Р°
РiСђРsРёРsРІС,РSCІС,Рё.

Р"РsСђРsСІР»С-

РѹСђРё РSPµРsР±С...С-РrРSPsСІС,С- РiСђРµРiР°СђР°С, Р'С-РІР°РNСђСђР° СІР»С-Рr

P·P°CÍ'C,PsCÍ'PsPICrPIP°C,Pë P·P° 1 PiPsPrPëPSCr PrPs CÍ'PµPeCÍ'CrP°P»CHbPSPsC—
P°PeC,PëPIPSsCÍ'C,C-. P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° CÍ'C,P°PSPsPIPeC,CH 50 PjPi.
PhCÍ'PeC-P»CHbPePë PiCtjPë PsPrPSPsC†P°CÍ'PSPsPjCr P·P°CÍ'C,PsCÍ'CrPIP°PSPSC-
PiCtjPµPiP°CtjP°C,Cr P·C—P¶PµCt PIC-PrP±CÍ'PIP°C''C,CHbCÍ'CI P·P°C,CtjPëPjPeP°
P°P±CÍ'PsCtjP±C†C-C— C,P° CrPiPsPIC-P»CHbPSCtC''C,CHbCÍ'CI PµC,,PµPeC,
PiCtjPµPiP°CtjP°C,Cr (PrPëPI. CtjPsP·PrC-P» B«PαP°CtjPjP°PePsPeC-PSPµC,PëPeP°B»),
CtjPµPePsPjPµPSPPrPsPIP°PSPs P·P°CÍ'C,PsCÍ'PsPICrPIP°C,Pë PiCtjPµPiP°CtjP°C, PSP°C,C%Pµ.

P—P°P»PµP¶PSPs PIC-Pr PµC,,PµPeC,PëPIPSsCÍ'C,C- C,P° PiPµCtjPµPSPsCÍ'PëPjPsCÍ'C,C-
PrPsP·Cr PiCtjPµPiP°CtjP°C,Cr PjPsP¶PSP° P·P±C-P»CHbCëPëC,Pë PrPs 100 PjPi P°P±Ps
P·PjPµPSCëPëC,Pë PrPs 25 PjPi*. PëP°PeCÍ'PëPjP°P»CHbPSP° CtjPµPePsPjPµPSPPrPsPIP°PSP°
PrPsP·P° CÍ'C,P°PSPsPIPeC,CH 100 PjPi.

PëP°PeCÍ'PëPjP°P»CHbPSP° CtjPµPePsPjPµPSPPrPsPIP°PSP° C†P°CÍ'C,PsC,P°
P·P°CÍ'C,PsCÍ'CrPIP°PSPSC CI PiCtjPµPiP°CtjP°C,Cr CÍ'C,P°PSPsPIPeC,CH 1 CtjP°P· PSP°
PrPsP±CÍ'.

PµP°C†C-C''PSC,Pë P»C-C,PSCHbPsPiPs PIC-PeCé

PkPµPsP±C...C-PrPSC-CÍ'C,CH Cr PePsCtjPµPeC†C-C— PrPsP·Pë PiP°C†C-C''PSC,P°Pj
P»C-C,PSCHbPsPiPs PIC-PeCÍ' (PIC-PePsPj PIC-Pr 65 CtjPsPeC-PI) PIC-PrCÍ'CrC,PSC CI.

PµP°C†C-C''PSC,Pë P·PSPëCtjPePsPIPsCt PSPµPrPsCÍ'C,P°C,PSC-CÍ'C,Ct

P''P»CI PiP°C†C-C''PSC,C-PI C-P·PSPëCtjPePsPIPsCt PSPµPrPsCÍ'C,P°C,PSC-CÍ'C,Ct
P»PµPiPePsPiPs C,P° PiPsPjC-CtjPSPsPiPs CÍ'C,CrPiPµPSC CI C,CI¶¶PePsCÍ'C,C-
(PeP»C-CtjPµPSCÍ' PeCtjPµP°C,PëPSC-PSCr 30Btj''80 PjP»/C...PI) CtjPµPePsPjPµPSPPrPsPIP°PSP°
PrPsP·P° PiCtjPµPiP°CtjP°C,Cr C'' C,P°PePsCt P¶, CI¶Pe PSP°PIPµPrPµPSPs PIPeC%Pµ Cr
CtjPsP·PrC-P»C- B«P''PsCtjPsCÍ'P»C-B».

PhCÍ'PeC-P»CHbPePë Cr PiP°C†C-C''PSC,C-PI P·PSPëCtjPePsPIPsCt
PSPµPrPsCÍ'C,P°C,PSC-CÍ'C,Ct C,CI¶¶¶PePsPiPs CÍ'C,CrPiPµPSC CI (PeP»C-CtjPµPSCÍ'
PeCtjPµP°C,PëPSC-PSCr < 30 PjP»/C...PI) PeP»C-CtjPµPSCÍ' CÍ'PëP»PrPµPSP°C,,C-P»Cr
P·PSPëP¶PµPSPëPñ, CÍ'P»C-Pr CtjPsP·PiP»CI¶PSCrC,Pë PjPsP¶P»PëPIC-CÍ'C,CH
P·P°CÍ'C,PsCÍ'CrPIP°PSPSC CI PrPsP·Pë B B B B B 25 PjPi*. P—P°P»PµP¶PSPs PIC-Pr
PµC,,PµPeC,PëPIPSsCÍ'C,C- C,P° PiPµCtjPµPSPsCÍ'PëPjPsCÍ'C,C- PiCtjPµPiP°CtjP°C,Cr PiCtjPë
PSPµPsP±C...C-PrPSPsCÍ'C,C- PrPsP·Cr PjPsP¶PSP° PiPsCÍ'C,CrPiPsPIPs P·P±C-P»CHbCëPëC,Pë
PrPs 50 PjPi C,P° PrPs 100 PjPi.

PµP°C†C-C''PSC,Pë P·PiPµC†C-PSPePsPIPsCt PSPµPrPsCÍ'C,P°C,PSC-CÍ'C,Ct

PhCÍ'PeC-P»CHbPePë Cr PiP°C†C-C''PSC,C-PI C-P·PiPµC†C-PSPePsPIPsCt
PSPµPrPsCÍ'C,P°C,PSC-CÍ'C,Ct (PSP°PiCtjPëPeP»P°Pr, C-P·C†PëCtjPsP·PsPj) PeP»C-CtjPµPSCÍ'
CÍ'PëP»PrPµPSP°C,,C-P»Cr P·PSPëP¶PµPSPëPñ, CÍ'P»C-Pr CtjPsP·PiP»CI¶PSCrC,Pë
PjPsP¶P»PëPIC-CÍ'C,CH P·P°CÍ'C,PsCÍ'CrPIP°PSPSC CI PrPsP·Pë 25 PjPi*. P—P°P»PµP¶PSPs PIC-Pr
PµC,,PµPeC,PëPIPSsCÍ'C,C- C,P° PiPµCtjPµPSPsCÍ'PëPjPsCÍ'C,C- PiCtjPµPiP°CtjP°C,Cr PiCtjPë
PSPµPsP±C...C-PrPSPsCÍ'C,C- PrPsP·Cr PjPsP¶PSP° PiPsCÍ'C,CrPiPsPIPs P·P±C-P»CHbCëPëC,Pë
PrPs 50 PjPi C,P° PrPs 100 PjPi.

*PµP°C†C-C''PSC,Pë, CI¶PeC- P·P°CÍ'C,PsCÍ'PsPICéCtC,CH C-PSCëC- P»C-PeP°CtjCÍ'CHbPeC-
P·P°CÍ'PsP±Pë*

PiPeC%Ps PiP°C†C-C''PSC,Pë PsPrPSPsC†P°CÍ'PSPs P·P°CÍ'C,PsCÍ'PsPICrCtC,CH

C-PSPIc-P±C-C,PsCḡPë CYP3A4 (PrPëPI. CḡPsP·PrC-P» B«P'P·P°C''PjPsPrC-Cḡ P· C-PSC€PëPjPë P»C-PeP°CḡCḡCHPePëPjPë P·P°CḡPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C''PjPsPrC-PNëB»), CḡP»C-Pr CḡPsP·PiP»CḡPSCrC,Pë PjPsPḡP»PëPIC-CḡC,CH P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PİPsC†P°C,PePsPIPsC— PrPsP·Pë 25 PjPi* (P·P° PIPëPSCḡC,PePsPj CḡPëC,PsPSP°PIC-CḡCḡ, P·P°CḡC,PsCḡCḡPIP°PSPSCḡ CḡPePsPiPs PsPrPSPsC†P°CḡPSPs P·C- CḡPëP»PrPµPSP°C,,C-P»PsPj PSPµ CḡPµPePsPjPµPSPrCḡC''C,CHCḡCḡ, PrPëPI. CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PsCḡCḡPIP°PSPSCḡB»).

PḡPµCḡPµP· CḡPëP·PëPe CḡPsP·PIPëC,PeCḡ PİPsCḡC,CḡCḡP°P»CHPSPsC— PiC-PİPsC,PµPSP·C-C— Cḡ PİP°C†C-C''PSC,C-PI, CḡPeC- P·P°CḡC,PsCḡPsPICḡCḡC,CH P±P»PsPeP°C,PsCḡPë α-P°PrCḡPµPSPsCḡPµC†PµPiC,PsCḡC-PI, PrPs PİPsC†P°C,PeCḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ CḡPëP»PrPµPSP°C,,C-P»Cḡ CḡP»C-Pr CḡPİPµPIPSPëC,PëCḡCḡ, C%Ps C—C...PSC-PNë CḡC,P°PSB CḡC,P°P±C-P»CHPSPëPNë. PḡP°PePsPḡ PİPsC,CḡC-P±PSPs CḡPsP·PiP»CḡPSCrC,Pë PjPsPḡP»PëPIC-CḡC,CH P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PİPsC†P°C,PePsPIPsC— PrPsP·Pë 25 PjPi* (PrPëPI. CḡPsP·PrC-P»Pë B«P'P·P°C''PjPsPrC-Cḡ P· C-PSC€PëPjPë P»C-PeP°CḡCḡCHPePëPjPë P·P°CḡPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C''PjPsPrC-PNëB» C,P° B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PsCḡCḡPIP°PSPSCḡB»).

*B P—P°CḡC,PsCḡPsPICḡPIP°C,Pë Cḡ PIC-PrPİPsPIC-PrPSPsPjCḡ PrPsP·CḡPIP°PSPSC-.

P''C-C,Pë.

PµCḡPµPİP°CḡP°C, PSPµ PİPsPeP°P·P°PSPëPNë PrPs P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PsCḡPsP±P°Pj PIC-PePsPj PrPs 18 CḡPsPeC-PI.

PµPµCḡPµPrPsP·CḡPIP°PSPSCḡ.

Pj PİCḡPsC†PµCḡC- PeP»C-PSC-C†PSPëC... PrPsCḡP»C-PrPḡPµPSCḡ P·P° CḡC†P°CḡC,CH PrPsCḡPsCḡP»PëC... PrPsP±CḡPsPIPsP»CHC†C-PI PİC-CḡP»Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PsPrPSPsCḡP°P·PsPIPsC— PrPsP·Pë CḡPëP»PrPµPSP°C,,C-P»Cḡ PrPs 800 PjPi PİPsP±C-C†PSC- CḡPµP°PeC†C-C— P±CḡP»Pë PİPsPrC-P±PSPëPjPë PrPs C,PëC..., C%Ps CḡPİPsCḡC,PµCḡC-PİP°P»PëCḡCḡ PİCḡPë P·P°CḡC,PsCḡCḡPIP°PSPSC- CḡPëP»PrPµPSP°C,,C-P»Cḡ Cḡ PSPëPḡC†PëC... PrPsP·P°C..., P°P»Pµ PIPëPSPëPeP°P»Pë C†P°CḡC,C-C€Pµ C,P° P±CḡP»Pë P±C-P»CHC€ C,CḡPḡPePëPjPë. P—P°CḡC,PsCḡCḡPIP°PSPSCḡ CḡPëP»PrPµPSP°C,,C-P»Cḡ Cḡ PrPsP·C- 200 PjPi PSPµ PİCḡPëP·PIPsPrPëP»Ps PrPs PİC-PrPIPëC%PµPSPSCḡ PµC,,PµPeC,PëPIPsPSCḡC,C-, P°P»Pµ CḡPİCḡPëC†PëPSCḡP»Ps P·CḡPsCḡC,P°PSPSCḡ PeC-P»CHPePsCḡC,C- PIPëPİP°PrPeC-PI CḡPsP·PIPëC,PeCḡ PİPsP±C-C†PSPëC... CḡPµP°PeC†C-PNë (PİPsP»PsPIPsPİPs P±PsP»CH, PİCḡPëPİP»PëPIC-PI PeCḡPsPIC-, P·P°PİP°PjPsCḡPsC†PµPSPSCḡ, PrPëCḡPİPµPİCḡC-C—, P·P°PeP»P°PrPµPSPsCḡC,C- PSPsCḡP°, PİPsCḡCḡC€PµPSCḡ P· P±PsPeCḡ PsCḡPİP°PSC-PI P·PsCḡCḡ).

Pj CḡP°P·C- PİPµCḡPµPrPsP·CḡPIP°PSPSCḡ PİCḡPë PSPµPsP±C...C-PrPSPsCḡC,C- PIPrP°CḡC,CHCḡCḡ PrPs P·PIPëC†P°PNëPSPëC... PİC-PrC,CḡPëPjCḡPIP°P»CHPSPëC... P·P°C...PsPrC-PI. PµCḡPëCḡPePsCḡPµPSPSCḡ PeP»C-CḡPµPSCḡCḡ CḡPëP»PrPµPSP°C,,C-P»Cḡ PİCḡPë PİPµPjPsPrC-P°P»C-P·C- PjP°P»PsPNëPjPsPIC-CḡPSPµ C†PµCḡPµP· PIPëCḡPsPePëPNë CḡC,CḡPİC-PSCḡ P·PİBḡ™ CḡP·CḡPIP°PSPSCḡ PİCḡPµPİP°CḡP°C,Cḡ P· P±C-P»PeP°PjPë PİP»P°P·PjPë PeCḡPsPIC- C,P° PIC-PrCḡCḡC,PSC-CḡC,CH PµP»C-PjC-PSP°C†C-C— CḡPëP»PrPµPSP°C,,C-P»Cḡ C-P· CḡPµC†PµCH.

PμPsP±C-C‡PSC- CḡPμP°PeC†C-C—.

PμCḡPsC,,C-P»CH P±PμP·PīPμPePē CÍPēP»PrPμPSP°C,,C-P»CÍ P±P°P·CÍC”C,CHCÍCÍ PSP°
PrP°PSPēC..., PsC,CḡPēPjP°PSPēC... C-P· 74 PīPsPrPIC-PNēPSPēC... CÍP»C-PīPēC...
PīP»P°C†PμP±Ps-PePsPSC,CḡPsP»CHPsPIP°PSPēC... PeP»C-PSC-C‡PSPēC...
PrPsCÍP»C-PrP¶PμPSCH (9570 PīP°C†C-C”PSC,C-PI). PḡP°PNēC‡P°CÍC,C-CēPμ
PīPsPIC-PrPsPjP»CÍP»PsCÍCÍ PīCḡPs C,P°PeC- PīPsP±C-C‡PSC- CḡPμP°PeC†C-C—, CÍPe
PīPsP»PsPIPSēPNē P±C-P»CH, PīCḡPēPīP»PēPIPē PeCḡPsPIC-, PrPēCÍPīPμPīCÍC-CÍ,
P·P°PeP»P°PrPμPSC-CÍC,CH PSPsCÍP°, P±C-P»CH CÍ CÍPīPēPSC-,
P·P°PīP°PjPsCḡPsC‡PμPSPSCÍ, PSCÍPrPsC,P°, PīCḡPēPīP»PēPIPē P¶P°CḡCÍ,
PīPsCḡCÍCēPμPSPSCÍ P·PsCḡCÍ, C†C-P°PSPsPīCÍC-CÍ C,P° P·P°C,CHPjP°CḡPμPSPSCÍ
P·PsCḡCÍ. P†PSC,,PsCḡPjP°C†C-CÍ C%PsPrPs PīPsP±C-C‡PSPēC... CḡPμP°PeC†C-PNē CÍ
CḡP°PjPeP°C... PīPsCÍC,PjP°CḡPePμC,PēSPiPsPIPsPīPs CÍPīPsCÍC,PμCḡPμP¶PμPSPSCÍ
P±CÍP»P° P·C-P±CḡP°PSP° PīCḡPsC,CÍPiPsPj PīPμCḡC-PsPrCÍ C,CḡPēPIP°P»C-CÍC,Cḡ
P±C-P»CHCēPμ PSC-P¶ 10 CḡPsPeC-PI. PhCÍPeC-P»CHPePē P·P°CÍPIPSēPePsPIC-
PīPsPIC-PrPsPjP»CÍP»PsCÍCÍ PSPμ PīCḡPs PICÍC- PīPsP±C-C‡PSC- CḡPμP°PeC†C-C— C,P°
PSPμ PICÍC- PīPsP±C-C‡PSC- CḡPμP°PeC†C-C— P±CÍP»Pē PīPeP»CḡC‡PμPSC- PI P±P°P·CÍ
PrP°PSPēC... P· P±PμP·PīPμPePē, C‡P°CÍC,PsC,P° C,P°PePēC... CḡPμP°PeC†C-PNē PSPμ PjPsP¶Pμ
P±CÍC,Pē PrPsCÍC,PsPIC-CḡPSPs PIPēP·PSP°C‡PμPSP°.

PjCÍC- PeP»C-PSC-C‡PSPs P·PSP°C‡CÍC%C- PīPsP±C-C‡PSC- CḡPμP°PeC†C-C—, C%Ps
CÍPīPsCÍC,PμCḡC-PiP°P»PēCÍCÍ PīC-Pr C‡P°CÍ PeP»C-PSC-C‡PSPēC...
PrPsCÍP»C-PrP¶PμPSCH C‡P°CÍC,C-CēPμ, PSC-P¶ PīCḡPē P·P°CÍC,PsCÍCÍPIP°PSPSC-
PīP»P°C†PμP±Ps, PSP°PIPμPrPμPSPs PSPēP¶C‡Pμ P·P° CÍPēCÍC,PμPjP°PjPē PsCḡPiP°PSC-PI C,P°
C‡P°CÍC,PsC,PsCḡ: PrCÍP¶Pμ C‡P°CÍC,Ps (≥1/10), C‡P°CÍC,Ps (≥1/100 вḡ” <1/10),
PSPμC‡P°CÍC,Ps (≥1/1000 вḡ” <1/100), CḡC-PrPePs (≥1/10000 вḡ” <1/1000), PrCÍP¶Pμ
CḡC-PrPePs (<1/10000), C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP° (PSPμ PjPsP¶Pμ P±CÍC,Pē
PICÍC,P°PSPsPIP»PμPSP° PIPēC...PsPrCÍC‡Pē P· PSP°CÍPIPSēC... PrP°PSPēC...
PḡP°CÍC,PsC,P° PeP»C-PSC-C‡PSPs P·PSP°C‡CÍC%PēC... PīPsP±C-C‡PSPēC... CḡPμP°PeC†C-PNē,
PīCḡPs CÍPeC- PīPsPIC-PrPsPjP»CÍP»PsCÍCÍ CÍ CḡP°PjPeP°C...
PīPsCÍC,PjP°CḡPePμC,PēSPiPsPIPēC... CÍPīPsCÍC,PμCḡPμP¶PμPSCH, PIPēP·PSP°C‡PμPSP°
CÍPe PSPμPIC-PrPsPjP°. Pj PjPμP¶P°C... PePsP¶PSPsC— PīCḡCÍPīPē P·P° C‡P°CÍC,PsC,PsCḡ
PīPsP±C-C‡PSC- CḡPμP°PeC†C-C— PSP°PIPμPrPμPSC- CÍ PīPsCḡCÍPrPeCÍ
P·PjPμPSCēPμPSPSCÍ C—C... CÍPμCḡPNēPsP·PSPsCÍC,C-.

P†PSC,,PμPeC†C-PNēPSC- C,P° C-PSPIP°P·PēPIPS- P·P°C...PIPsCḡCḡPIP°PSPSCÍ

PḡPμC‡P°CÍC,Ps: CḡPēPSC-C,.

P— P±PsPeCž C-PjCžPSPSPsC— CÍPēCÍC,PμPjPē

PḡPμC‡P°CÍC,Ps: CḡPμP°PeC†C-C— PīC-PrPIPēC%PμPSPsC— C‡CÍC,P»PēPIPsCÍC,C-.

P— P±PsPeCž PSPμCḡPIPsPIPsC— CÍPēCÍC,PμPjPē

P”CÍP¶Pμ C‡P°CÍC,Ps: PīPsP»PsPIPSēPNē P±C-P»CH.

PḡP°CÍC,Ps: P·P°PīP°PjPsCḡPsC‡PμPSPSCÍ.

PḡPμC‡P°CÍC,Ps: CÍPsPSP»PēPIC-CÍC,CH, PīC-PīPμCÍC,PμP·C-CÍ.

P C-PrPePs: C-PSCÍCíP»CHC,, CÍPëPSPePsPíPµ, C,CĤP°PSP·PëC,PsCĤPSP° C-CëPµPjC-C†PSP° P°C,P°PeP°, CÍCíPrPsPjPë, CĤPµC†PëPrPëPIPë CÍCíPrPsPj.

P— P±PsPeCž PsCĤPiP°PSC-PI P·PsCĤCž

PŞP°CÍC,Ps: PíPsCĤCíCëPµPSPSCİ CÍPíCĤPëPNëPSCİC,C,Cİ PëPsP»CHPsCĤCí*, CĤPsP·P»P°PrPë P·PsCĤCí, P·P°C,CHPjP°CĤPµPSPSCİ P·PsCĤCí.

PќPµC†P°CÍC,Ps: CĤPsP·P»P°PrPë CÍP»CHPsP·PsPIPëPrC-P»PµPSPSCİ**, P±C-P»CH PI PsC†P°C..., C,,PsC,PsC,,PsP±C-Cİ, C,,PsC,PsPíCÍC-Cİ, PiC-PíPµCĤPµPjC-Cİ PsC†PµPNë, CİCÍPëCĤP°PIC-CÍC,CH P·PsCĤCí, PePsPSbĤ™ CĤPSPeC,PëPIC-C,,.

P C-PrPePs: PSPµP°CĤC,PµCĤC-P°P»CHPSP° PíPµCĤPµPrPSCİ C-CëPµPjC-C†PSP° PSPµPNëCĤPsPíP°C,C-Cİ P·PsCĤPsPIPsPíPs PSPµCĤPIP°, PsPeP»CHP·C-Cİ CÍCíPrPëPS CÍC-C,PeC-PIPePë, CĤPµC,PëPSP°P»CHPSPëPNë PeCĤPsPIPsPIPëP»PëPI, P°CĤC,PµCĤC-PsCÍPeP»PµCĤPsC,PëC†PSP° CĤPµC,PëPSPsPíP°C,C-Cİ, PíPsCĤCíCëPµPSPSCİ P· P±PsPeCí CÍC-C,PeC-PIPePë, PiP»P°CíPePsPjP°, PrPµC,,PµPeC,Pë PíPsP»Cİ P·PsCĤCí, PrPëPíP»PsPíC-Cİ, P·PSPëP¶PµPSPSCİ PiPsCÍC,CĤPsC,Pë P·PsCĤCí, PjC-PsPíC-Cİ, P°CÍC,PµPSPsPíC-Cİ, PíP»P°PIP°CĤC†C- PíPsPjCíC,PSC-PSPSCİ CÍPeP»PëCÍC,PsPiPs C,C-P»P°, PíPsCĤCíCëPµPSPSCİ P· P±PsPeCí CĤP°PNëPrCíP¶PSPsC— PsP±PsP»PsPSPePë, PjC-PrCĤC-P°P, PíPsCİPIP° CÍCİCĤC†PëC... PeCĤCíPiC-PI PSP°PIPePsP»Ps PrP¶PµCĤPµP»P° CÍPIC-C,P»P° (PiP°P»Ps) Cí PíPsP»C- P·PsCĤCí, PSP°P±CĤCİPe PsC†PµPNë, PíCĤPëPíCíC...P»C-CÍC,CH PsC†PµPNë, PíPsCĤCíCëPµPSPSCİ P· P±PsPeCí PsC†PµPNë, PiC-PíPµCĤPµPjC-Cİ PePsPSbĤ™ CĤPSPeC,PëPIPë, PíPsPrCĤP°P·PSPµPSPSCİ PsC†PµPNë, P°PSPsPjP°P»CHPSC- PIC-PrC†CíC,C,Cİ PI PsC†P°C..., PSP°P±CĤCİPe PíPsPIC-Pe, P·PSPµP±P°CĤPIP»PµPSPSCİ CÍPeP»PµCĤPë.

P— P±PsPeCž PsCĤPiP°PSC-PI CÍP»CžC...Cž C,P° PIPµCÍC,PëP±CžP»CİCĤPSPsPiPs P°PíP°CĤP°C,Cž

PќPµC†P°CÍC,Ps: P·P°PíP°PjPsCĤPsC†PµPSPSCİ, PIPµCĤC,PëPiPs, PrP·PIC-PS Cí PICíC...P°C....

P C-PrPePs: PiP»CíC...PsC,P°.

P— P±PsPeCž CÍPµCĤC†PµPIPs-CÍCžPrPëPSPSPsC— CÍPëCÍC,PµPjPë

PŞP°CÍC,Ps: PíCĤPëPíP»PëPIPë PeCĤPsPIC- PrPs PsP±P»PëC†C†Cİ, PíCĤPëPíP»PëPIPë P¶P°CĤCí.

PќPµC†P°CÍC,Ps: C,P°C...C-PeP°CĤPrC-Cİ, PíPsCÍPëP»PµPSPµ CÍPµCĤC†PµP±PëC,C,Cİ, P°CĤC,PµCĤC-P°P»CHPSP° PiC-PíPµCĤC,PµPSP·C-Cİ, P°CĤC,PµCĤC-P°P»CHPSP° PiC-PíPsC,PµPSP·C-Cİ.

P C-PrPePs: CĤP°PíC,PsPIP° CÍPµCĤC†PµPIP° CÍPjPµCĤC,CH, C-PSC,,P°CĤPeC, PjC-PsPeP°CĤPrP°, CëP»CíPSPsC†PePsPIP° P°CĤPëC,PjC-Cİ, C,,C-P±CĤPëP»CİC†C-Cİ PíPµCĤPµPrCÍPµCĤPrCH, PSPµCÍC,P°P±C-P»CHPSP° CÍC,PµPSPsPeP°CĤPrC-Cİ.

P— P±PsPeCž PrPëC...P°P»CHPSPsC— CÍPëCÍC,PµPjPë, PiCĤCžPrPSPsC— PeP»C-C,PePë C,P° CÍPµCĤPµPrPsCÍC,C-PSPSCİ

PŞP°CÍC,Ps: P·P°PeP»P°PrPµPSC-CÍC,CH PSPsCÍP°.

PќPµC†P°CÍC,Ps: PSPsCÍPsPIP° PeCĤPsPIPsC,PµC†P°, P·P°PeP»P°PrPµPSC-CÍC,CH

ΠΪCΉPēPrP°C,PePsPIPēC... ΠiP°P·CfC... PSPsCfP°.

P C-PrPePs: PIC-PrC‡CfC,C,Cf CfC,PēCfPSPμPSPSCf Cf ΠiPsCΉP»C-, PSP°P±CΉCfPe CfP»PēP·PsPIPsC— PsP±PsP»PsPSPePē PSPsCfP°, CfCfC...C-CfC,CΉ Cf PSPsCfC-.

P— P±PsPeCζ CēP»CζPSPePsPIPs-PePēCēPePsPIPsΠiPs C,CΉP°PeC,Cζ

P§P°CfC,Ps: PSCfPrPsC,P°, PrPēCfΠiPμΠiCfC-Cf.

PκPμC‡P°CfC,Ps: ΠiP°CfC,CΉPsPμP·PsC,,P°ΠiPμP°P»CΉPSP° CΉPμC,,P»CΉPeCfPSP° C...PIPsCΉPsP±P°, P±P»CΉPIP°PSPSCf, P±C-P»CΉ Cf ΠiPμCΉC...PSC-PMζ C‡P°CfC,PēPSC-P¶PēPIPsC,P°, CfCfC...C-CfC,CΉ Cf CΉPsC,C-.

P C-PrPePs: ΠiC-ΠiPμCfC,PμP·C-Cf CΉPsC,PsPIPsC— ΠiPsCΉPsP¶PSPēPSPē.

P— P±PsPeCζ CēPeC-CΉPē C,P° ΠiC-PrCēPeC-CΉPSPsC— PeP»C-C,PePsPIPēPSPē

PκPμC‡P°CfC,Ps: PIPēCfPēΠiP°PSPSCf.

P C-PrPePs: CfPēPSPPrCΉPsPj PŸC,C-ΠiPμPSCfP°BΉ“P”P¶PsPSCfPsPSP°, C,PsPeCfPēC‡PSPēPMζ PμΠiC-PrPμCΉPjP°P»CΉPSPēPMζ PSPμPeCΉPsP»C-P·.

P— P±PsPeCζ PsΠiPsCΉPSPs-CΉCζC...PsPIPsΠiPs P°ΠiP°CΉP°C,Cζ C,P° CfΠiPsP»CζC‡PSPsC— C,PeP°PSPēPSPē

PκPμC‡P°CfC,Ps: PjC-P°P»ΠiC-Cf, P±C-P»CΉ Cf PeC-PSC‡C-ΠiPeP°C....

P— P±PsPeCζ CfPμC‡PsPIPēPrC-P»CΉPSPsC— CfPēCfC,PμPjPē

PκPμC‡P°CfC,Ps: ΠiPμPjP°C,CfCΉC-Cf.

P— P±PsPeCζ CΉPμΠiCΉPsPrCζPeC,PePIPsPsC— CfPēCfC,PμPjPē C,P° PjPsP»PsC‡PSPēC... P·P°P»PsP·

P C-PrPePs: PeCΉPsPIPsC,PμC‡P° P·C- CfC,P°C,PμPIPsΠiPs C‡P»PμPSP°, ΠiCΉC-P°ΠiC-P·Pj, ΠiPμPjP°C,PsCfΠiPμCΉPjC-Cf, ΠiPsPrPsPIP¶PμPSP° PμCΉPμPeC‡C-Cf.

P— P°ΠiP°P»CΉPSC- CΉPsP·P»P°PrPē C,P° CΉPμP°PeC‡C-C— Cζ PjC-CfC‡C- ΠiΠiPμPrPμPSPSCf

PκPμC‡P°CfC,Ps: P±C-P»CΉ Cf ΠiCΉCfPrCfC..., ΠiC-PrPIPēC%PμPSP° PIC,PsPjP»CΉPIP°PSC-CfC,CΉ, PIC-PrC‡CfC,C,Cf P¶P°CΉCf.

P C-PrPePs: ΠiPsPrCΉP°P·PSPμPSPSCf.

P>P°P±PsCΉP°C,PsCΉPSC- C,PμCfC,Pē

PκPμC‡P°CfC,Ps: ΠiC-PrPIPēC%PμPSP° C‡P°CfC,PsC,P° CfPμCΉC‡PμPIPēC... CfPePsCΉPsC‡PμPSCΉ.

* B PμPsCΉCfCēPμPSPSCf CfΠiCΉPēPMζPSCfC,C,Cf PePsP»CΉPsCΉCf: C...P»PsCΉPsΠiCfC-Cf, C...CΉPsPjP°C,PsΠiCfC-Cf, C‡C-P°PSPsΠiCfC-Cf, PμCΉPēC,CΉPsΠiCfC-Cf, PeCfP°PSC,PsΠiCfC-Cf.

** PμPsCΉCfCēPμPSPSCf CfP»CΉPsP·PsPIPēPrC-P»PμPSPSCf: CfCfC...C-CfC,CΉ Πi

PsC†P°C..., PīPsCḡCfC€PμPSPSCḡ C†P»CHbPsP·PsPIPëPrC-P»PμPSPSCḡ C,P°
PīC-PrPIPëC%PμPSPSCḡ C†P»CHbPsP·PsPIPëPrC-P»PμPSPSCḡ.

PkPëP¶C†PμP·P°P·PSP°C†PμPSC- CḡIPIPëC%P° C†PīPsC†C,PμCḡC-PiP°P»PëC†Cḡ C† < 2 %
PīP°C†C-C"°PSC,C-PI C† PīCḡPsC†PμC†C- PePsPSC,CḡPsP»CHbPsPIP°PSPëC...
PeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP¶PμPSCḡ; PīCḡPëC†PëPSPSPëPNë
PIP·P°C"°PjPsP·PIbḡ™ CḡP·PsPe PSPμ PIPëP·PSP°C†PμPSPëPNë. PμPsPIC-PrPsPjP»PμPSPSCḡ
PIPeP»CHC†P°P»Pë CḡIPIPëC%P°, C%Ps PjP°P»Pë PIC-CḡPsPiC-PrPSPëPNë P·PIbḡ™ CḡP·PsPe
C-P· P·P°C†C,PsC†C†PIP°PSPSCḡPj PīCḡPμPīP°CḡP°C,C†. PīIPIPëC%P°, CḡPeC- PSPμ P±C†P»Pë
P·P°P·PSP°C†PμPSC-, P±C†P»Pë P»PμPiPePëPjPë C,P° PīPsPIC-PrPsPjP»PμPSPSCḡ P±C†P»Pë
PrC†P¶Pμ PSPμC,PsC†PSPëPjPë, C%PsP± PjP°C,Pë P·PSP°C†PμPSPSCḡ.

P—P°PiP°P»CHbPSC-. PkP°P±CḡCḡPe PsP±P»PëC†C†Cḡ, CḡPμP°PeC†C-C—
C,,PsC,PsC†C†C,P»PëPIPsC†C,C-, C€PsPe, P°C†C,PμPSC-Cḡ, P±C-P»CHb, CḡP°PiC,PsPIPμ
PīP°PrC-PSPSCḡ, P±C-P»CHb C† P¶PëPIPsC,C-, CḡP°PiC,PsPIPμ PīPsC€PePsPrP¶PμPSPSCḡ.

P— P±PsPeCž C†PμCḡC†PμPIPs-C†CžPrPëPSPSPsC— C†PëC†C,PμPjPë:
C†C,PμPSPsPeP°CḡPrC-Cḡ, PḡV-P±P»PsPeP°PrP°, PjC-PiCḡPμPSCḡ, PīPsC†C,C†CḡP°P»CHbPSP°
PiC-PīPsC,PμPSP·C-Cḡ, C-C€PμPjC-Cḡ PjC-PsPeP°CḡPrP°, C,CḡPsPjP±PsP· C†C†PrPëPS
PīPsP»PsPIPSPsPiPs PjPsP·PeC†, CḡP°PiC,PsPIP° P·C†PīPëPSPeP° C†PμCḡC†Cḡ,
PIC-PrC...PëP»PμPSPSCḡ PīPsPeP°P·PSPëPeC-PI P·PḡP", PeP°CḡPrC-PsPjC-PsPīP°C,C-Cḡ.

P— P±PsPeCž C€P»CžPSPePsPIPs-PePëC€PePsPIPsPiPs C,CḡP°PeC,Cž: PiP»PsC†PëC,, PePsP»C-C,,
PrPëC†C,,P°PiC-Cḡ, PiP°C†C,CḡPëC,, PiP°C†C,CḡPsPμPSC,PμCḡPëC,, PμP·PsC,,P°PiC-C,,
C†C,PsPjP°C,PëC,, PīPsCḡCfC€PμPSPSCḡ CḡPμP·C†P»CHbC,P°C,C-PI PīPμC†C-PSPePsPIPëC...
PīCḡPsP±, CḡPμPeC,P°P»CHbPSP° PeCḡPsPIPsC,PμC†P°, PiC-PSPiC-PIC-C,.

P— P±PsPeCž C†PëC†C,PμPjPë PeCḡPsPIC- C,P° P»C-PjC,,P°C,PëC†PSPsC— C†PëC†C,PμPjPë:
P°PSPμPjC-Cḡ, P»PμPNëPePsPīPμPSC-Cḡ.

P PsP·P»P°PrPë PjPμC,P°P±PsP»C-P·PjCž C,P° C...P°CḡC†CžPIP°PSPSCḡ: C†PīCḡP°PiP°,
PSP°P±CḡCḡPe, PīPsPrP°PiCḡP°, PSPμC†C,P°P±C-P»CHbPSPëPNë PrC-P°P±PμC,,
PiC-PīPμCḡPiP»C-PePμPjC-Cḡ, PīPμCḡPëC,,PμCḡPëC†PSC- PSP°P±CḡCḡPePë,
PiC-PīPμCḡCfCḡPëPePμPjC-Cḡ, PiC-PīPsPiP»C-PePμPjC-Cḡ, PiC-PīPμCḡPSP°C,CḡC-C"°PjC-Cḡ.

P— P±PsPeCž C†PePμP»PμC,PSPs-Pjēḡ™ CḡP·PsPIPsC— C†PëC†C,PμPjPë: P°CḡC,CḡPëC,,
P°CḡC,CḡPsP·, CḡPsP·CḡPëPI C†C†C...PsP¶PëP»P»Cḡ, C,PμPSPsC†PëPSPsPIC-C,, P±C-P»CHb C†
PeC-C†C,PeP°C..., PjC-P°C†C,PμPSC-Cḡ, C†PëPSPsPIC-C,.

P— P±PsPeCž PSPμCḡPIPsPIPsC— C†PëC†C,PμPjPë: P°C,P°PeC†C-Cḡ, PSPμPICḡP°P»PiC-Cḡ,
PSPμPNëCḡPsPīP°C,C-Cḡ, PīP°CḡPμC†C,PμP·C-Cḡ, C,CḡPμPjPsCḡ, PIPμCḡC,PëPiPs,
PrPμPiCḡPμC†C-Cḡ, P±PμP·C†PsPSPSCḡ, P°PSPsPjP°P»CHbPSC- C†PSPsPIPëPrC-PSPSCḡ,
P·PSPëP¶PμPSPSCḡ CḡPμC,,P»PμPeC†C-PI.

P— P±PsPeCž PrPëC...P°P»CHbPSPsC— C†PëC†C,PμPjPë: P°C†C,PjP°, PrPëC†PīPSPsPμ,
P»P°CḡPëPSPiC-C,, C,,P°CḡPëPSPiC-C,, C†PëPSC†C†PëC,, P±CḡPsPSC...C-C,, PīPsC†PëP»PμPSPμ
C†P»PëPSPsPIPëPrC-P»PμPSPSCḡ, PīPsC†PëP»PμPSPSCḡ PeP°C€P»Cḡ.

P PsP·P»P°PrPë P· P±PsPeCž C€PeC-CḡPë: PeCḡPsPīPëPIbḡ™ CḡPSPeP°, PiPμCḡPiPμC†,
C†PIPμCḡP±C-P¶, PīC-PrPIPëC%PμPSP° PīC-C,P»PëPIC-C†C,CHb, PIPëCḡP°P·PePë C€PeC-CḡPë,
PePsPSC,P°PeC,PSPëPNë PrPμCḡPjP°C,PëC,, PμPeC†C,,PsP»C-P°C,PëPIPSPëPNë PrPμCḡPjP°C,PëC,.

PŸPīPμC†PëC,,C-C†PSC- PIC-PrC†CžC,C,Cḡ: CḡP°PiC,PsPIPμ P·PSPëP¶PμPSPSCḡ C†Pë

PIC,C₇H₅P^oC,P^o C₇P^o»C₇C...C₇, P±C-P^o»CH₅ C₇ PIC₇C...P^oC..., PeC₇PsPIPsPIP₅P^o»P₅PI C₇ PsPePs,
PeP^oC,P^oC₇P^oPeC,P^o, C₇C₇C...C-C₇C,CH₅ PI PsC₇P^oC...

P— P±PsPeC₇ C₇C₇PsPiP₅PSC-C,P^oP^o»CH₅PSPsC— C₇P₅C₇C,P₅PjP₅: C₇P₅C₇C,P₅C,,
PSC-PeC,C₇C₇C-C₇, P₅C-PrPIP₅PeC₇PsP^o C₇P^oC₇C,PsC,P^o C₇P₅C₇PsPIP₅P₅C₇C₇P^oPSCH₅,
P·P±C-P^o»CH₅C₇PsPSPSC₇ PjPsP^o»PsC₇PSP₅PeC... P·P^oP^o»PsP·, PSP₅C₇C₇P₅PjP^oPSPSC₇ C₇P₅C₇C-,
P₅PsC₇C₇C₇PsPSPSC₇ P₅C₇PeC₇P^o»C₇C₇C-C-, PSP^oP±C₇C₇Pe C₇C,P^oC,P₅PIP₅PeC...
PsC₇PiP^oPSC-PI, P^oPSPsC₇PiP^oP·PjC-C₇.

P^oPsC₇PIC-Pr P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇ P₅C-C₇P^o»C₇ PIP₅PeC...PsPrC₇ PSP^o C₇P₅PePSPsPe.
P₅C-C₇P^o»C₇ PIP₅PeC...PsPrC₇ P₅C₇P₅P^oC₇P^oC, C₇ PSP^o C₇P₅PePSPsPe P±C₇P^o»P₅
C-PrP₅PSC,P₅C,,C-PePsPIP^oPSC- PSP₅P₅C₇P₅P^oP·PSP^oC₇P₅PSC- P₅PsP±C-C₇PSC-
C₇P₅P^oPeC₇C-C-. P₅C₇PeC-P^o»CH₅PeP₅ P₅C₇Ps C,P^oPeC- C₇P₅P^oPeC₇C-C-
P₅PsPIC-PrPsPjP^o»C₇C₇C,CH₅ PrPsP±C₇PsPIC-P^o»CH₅PSPs C,P^o P₅PsPIC-PrPsPjP^o»P₅PSPSC₇
PSP^oPrC...PsPrC₇C,CH₅ PIC-Pr P₅PsP₅C₇P^o»C₇C₇C-C- PSP₅PIC-PrPsPjPsC-
C₇P₅C₇P₅P^o»CH₅PSPsC₇C-, PSP₅ P·P^oPIP₅P₅P₅ PjPsP₅PSP^o PrPsC₇C,PsPIC-C₇PSPs
PsC₇C-PSP₅PeC, P₅C—C... C₇P^oC₇C,PsC,C₇ C,P^o PIC₇C,P^oPSPsPIP₅PeC,P₅ P₅C₇P₅PeC₇P₅PSP₅PeP₅
P·P₅PeC₇ C₇P·PsPe C-P· P₅PeC₇P₅PsP·P₅C₇C-C^oC₇ P^o»C-PeP^oC₇C₇CH₅PePsPiPs P·P^oC₇PsP±C₇.
P₅C- C₇PIP₅PeC₇P^o P±C₇P^o»P₅ P·P^oP·PSP^oC₇P₅PSC- C₇Pe C₇P₅C₇P₅P· C—C...
C₇P₅C₇P₅PeP₅PSC-C₇C,CH₅, C₇P^oC₇C,PsC,C₇ P₅PsPIC-PrPsPjP^o»P₅PSPSC₇,
PIC-PrC₇C₇C,PSC-C₇C,CH₅ C₇C-C,PePsPiPs P^oP^o»CH₅C,P₅C₇PSP^oC,P₅PIPSPsPiPs
P·P₅PeC₇ C₇P·PeC₇, C,P^oPe C- C₇P₅C₇P₅P· PePsPjP±C-PSP^oC₇C-C₇ C₇P₅PeC... C,,P^oPeC,PsC₇C-PI.

P₅P₅C₇C₇P₅PIPs-C₇C₇PrP₅PePSPSC- C,P^o C₇P₅C₇P₅P±C₇PsPIP^oC₇PeC₇P^o»C₇C₇PSC-
C₇PIP₅PeC₇P^o. P₅PsPIC-PrPsPjP^o»C₇P₅»PsC₇C₇ P₅C₇Ps C₇P₅C₇P₅PeP₅PSC- C₇P₅C₇C₇P₅PIPs-
C₇C₇PrP₅PePSPSC-, C₇P₅C₇P₅P±C₇PsPIP^oC₇PeC₇P^o»C₇C₇PSC- C,P^o C₇C₇PrP₅PePSPSC-
C₇PIP₅PeC₇P^o, PIP₅Pe^o»C₇C₇P^oC₇C₇P₅ C₇P₅C₇P₅P±C₇PsPIP^oC₇PeC₇P^o»C₇C₇PSC₇
PeC₇PsPIPsC,P₅C₇C₇, C₇C₇P±P^oC₇P^oC...PSPsC—PrP^oP^o»CH₅PSC₇ C,P^o
PIPSC₇C,C₇C-C₇PSCH₅PsC₇P₅C₇P₅P±C₇P^oP^o»CH₅PSC₇ PeC₇PsPIPsC,P₅C₇C₇ C,P^o
P^o»P₅PiP₅PSP₅PIC₇ PeC₇PsPIPsC,P₅C₇C₇, C₇Ps P±C₇P^o»P₅ P₅PsPiP₅PeC₇ C₇P·P^oPSC- C₇ C₇P^oC₇C-
C-P· P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇Pj C₇P₅Pe^o»PrP₅PSP^oC,,C-P^oC₇. Pj P±C-P^o»CH₅C₇PsC₇C,C-
P₅P^oC₇C-C^oPSC,C-PI P±C₇P^o»P₅ PSP^oC₇PIPSC- C,,P^oPeC,PsC₇P₅ C₇P₅C₇C₇P₅PIPs-
C₇C₇PrP₅PePSPSPsPiPs C₇P₅PeP·P₅PeC₇. P₅PsPIC-PrPsPjP^o»C₇P₅»PsC₇C₇, C₇Ps P±P^oPiP^oC,Ps P·
C₇P₅PeC... C₇PIP₅PeC₇ PIP₅PePSP₅PeP^o»P₅ P₅C-Pr C₇P^oC₇ P^oP±Ps PsPrC₇P^oP·C₇ P₅C-C₇P^o»C₇
C₇P₅PeC₇C₇P^o»CH₅PSPsC— P^oPeC,P₅PIPSPsC₇C,C- C,P^o PrP₅PeC-P^o»CH₅PeP^o C₇PIP₅PeC₇
PIP₅PePSP₅PeP^o»P₅ PsPrC₇P^oP·C₇ P₅C-C₇P^o»C₇ P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇
C₇P₅Pe^o»PrP₅PSP^oC,,C-P^oC₇ P±P₅P· C₇P₅PeC₇C₇P^o»CH₅PSPsC— P^oPeC,P₅PIPSPsC₇C,C-
P₅PSC₇C- C₇PIP₅PeC₇P^o PIP₅PePSP₅PeP^o»P₅ P₅C₇PsC,C₇PiPsPj PSP^oC₇C,C₇PiPSP₅PeC... P₅PsPrP₅PS
C₇P₅PrPSC-PI P₅C-C₇P^o»C₇ P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇ C₇P₅Pe^o»PrP₅PSP^oC,,C-P^oC₇ C,P^o
C₇P₅PeC₇C₇P^o»CH₅PSPsC— P^oPeC,P₅PIPSPsC₇C,C-. P₅P₅PjPsP₅P₅»P₅PIPs
PIC₇C,P^oPSPsPIP₅PeC,P₅, C₇P₅ C₇C- C₇PIP₅PeC₇P^o P₅PsPiP₅PeC₇ C₇P·P^oPSC- C-P·
P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇Pj P₅C₇P₅P₅P^oC₇P^oC, C₇-P· C₇P₅PeC₇C₇P^o»CH₅PSPsC₇
P^oPeC,P₅PIPSC-C₇C,C₇, C-P· PSP^oC₇PIPSP₅PeP₅ C,,P^oPeC,PsC₇P^oPjP₅ C₇P₅PeP·P₅PeC₇ C₇P₅ C-P·
PePsPjP±C-PSP^oC₇C-C^oC₇ C₇P₅PeC... C,,P^oPeC,PsC₇C-PI, C₇P₅ P· C-PSC₇PePjP₅
C,,P^oPeC,PsC₇P^oPjP₅.

P₅C₇PsPIPsPSPsC₇PSP^o C,P^o P^o»C-PjC,,P^oC,P₅PeC₇PSP^o C₇P₅C₇C,P₅PjP₅:
PIP^oP·PsPsPeP^o»CH₅P·P₅PIPSP₅PeP₅ PeC₇P₅P· Pj PSP₅PIP₅P₅»P₅PePsPjC₇ P·P^oPIC₇P^oC₇PSPs
P₅C₇P₅PiP₅PePSP₅PjC₇ PrPsC₇P^o»C-PrP₅P₅PSPSC- P·P^oC₇C,PsC₇C₇PIP^oPSPSC₇
P₅C₇P₅PiP^oC₇P^oC, C₇ C₇P₅Pe^o»PrP₅PSP^oC,,C-P^o P·P^o C₇C₇P^oC₇C,C₇ P₅P^oC₇C-C^oPSC,C-PI P·
P^o»P₅PiP₅PSP₅PIPsC₇ P^oC₇C,P₅C₇C-P^o»CH₅PSPsC₇ P₅C-PiP₅C₇C,P₅PSP·C-C^oC₇,
PIC,PsC₇P₅PePSPSPsC₇ C₇PsPrPs C₇P₅C₇P₅PiPsP₅PrC-P±PSPsPeP^o»C-C,P₅PePSPSPsC—

P°PSPμPjC—, PīCḡPē P·P°CíC,PsCíCíPíP°PSPSC— CíPēP»PrPμPSP°C,,C—P»Cí PīCḡPs
CḡPsP·PIPēC,PsPe PIP°P·PsPsPeP»CḡP·PēPIPSPēC... PeCḡPēP·C—PI, C%Ps
PīPsC,CḡPμP±CíPíP°P»Pē PíPsCíPíC—C,P°P»C—P·P°C†C—, PíPsPIC—PrPsPjP»CḡP»PsCíCḡ
C†P°CíC,C—CēPμ, PSC—Pḡ PīCḡPē P·P°CíC,PsCíCíPíP°PSPSC— PīP»P°C†PμP±Ps.
PḡP»C—PSC—C†PSPμ P·PSP°C†PμPSPSCḡ C†C—C”C— C—PSC,,PsCḡPjP°C†C— PrP»Cḡ
PīP°C†C—C”PSC,C—PI, CḡPeC— P·P°CíC,PsCíCíPíCíCḡC,Cḡ CíPēP»PrPμPSP°C,,C—P» P·
PjPμC,PsCḡ P»C—PeCíPíP°PSPSCḡ PμCḡPμPeC,PēP»CḡPSPsC— PrPēCíC,,CíPSPeC†C—C—,
PSPμPIC—PrPsPjPs.

P— P±PsPeCž PSPμCḡPIPSPiPsC— CíPēCíC,PμPjPē: C,CḡPēPIPSPiP°, C,CḡP°PSP·PēC,PsCḡPSP°
PíP»PsP±P°P»CḡPSP° P°PjPSPμP·C—Cḡ.

PŸPíPμC†PēC,,C—C†PSC— PIC—PrC†CžC,C,Cḡ

PŸP»CžC.... PμC—CíP»Cḡ PIPēC...PsPrCí PīCḡPμPíP°CḡP°C,Cí PSP° CḡPēPSPsPe
PíPsPIC—PrPsPjP»CḡP»PsCíCḡ PīCḡPs PIPēPíP°PrPePē CḡP°PíC,PsPIPSPiPs P·PSPēPḡPμPSPSCḡ
C†Pē PIC,CḡP°C,Pē CíP»CíC...Cí, PíPsPíBḡ™ CḡP·P°PSC— Cí C†P°CíC— C—P·
P·P°CíC,PsCíCíPíP°PSPSCḡPj CíPēP»PrPμPSP°C,,C—P»Cí. Pj PrPμCḡPePēC... PIPēPíP°PrPeP°C...
PíPsPIC—PrPsPjP»CḡP»PsCíCḡ PīCḡPs PSP°CḡPIPSC—CíC,Cḡ PjPμPrPēC†PSPēC... CíC,P°PSC—PI
C,P° C—PSCēPēC... C,,P°PeC,PsCḡC—PI, C%Ps PjPsPíP»Pē PIC—PrC—PíCḡP°C,Pē CḡPsP»Cḡ Cí
CḡPsP·PIPēC,PeCí PíPsP±C—C†PSPēC... CḡPμP°PeC†C—Pḡ P· P±PsPeCí CíP»CíC...Cí. Pj
P±P°PíP°C,CḡPsC... PIPēPíP°PrPeP°C... C—PSC,,PsCḡPjP°C†C—Cḡ C%PsPrPs
PíPsPrP°P»CḡCēPsPíPs PjPμPrPēC†PSPSPiPs CíPíPsCíC,PμCḡPμPḡPμPSPSCḡ
PIC—PrCíCíC,PSCḡ. P·PēP·PSP°C†PēC,Pē, C†Pē C†C— CḡPIPēC%P° PíCḡCḡPjPs
PíPsPíBḡ™ CḡP·P°PSC— C—P· P·P°CíC,PsCíCíPíP°PSPSCḡPj CíPēP»PrPμPSP°C,,C—P»Cí, P·
PSP°CḡPIPSPēPjPē C,,P°PeC,PsCḡP°PjPē CḡPēP·PēPeCí PIC,CḡP°C,Pē CíP»CíC...Cí, P·
PePsPjP±C—PSP°C†C—C”Cḡ C†PēC... C,,P°PeC,PsCḡC—PI C†Pē P· C—PSCēPēPjPē
C,,P°PeC,PsCḡP°PjPē, PSPμPjPsPḡP»PēPIPSP.

P—C—Cḡ. PŸPēPjC†P°CíPSPiP° PIC,CḡP°C,P° P·PsCḡCí, PíPsC†PμCḡPIPSPSC—PSPSCḡ PsC†PμPḡ,
PíPμC†C—PSPSCḡ Pí PsC†P°C..., PíC—PrPIPēC%PμPSPSCḡ PIPSCíC,CḡC—CēPSCḡPsPsC†PSPSPiPs
C,PēCíPeCí, PSP°P±CḡCḡPe CíC—C,PeC—PIPePē, CíCíPrPēPSPSC—
P·P°C...PIPSPCḡPIP°PSPSCḡ CíC—C,PeC—PIPePē C†Pē PeCḡPsPIPSP,C,PμC†P°,
PIC—PrCēP°CḡCíPíP°PSPSCḡ CíPeP»PēCíC,PsPíPs C,C—P»P°.

PμC—CíP»Cḡ PIPēC...PsPrCí PīCḡPμPíP°CḡP°C,Cí PSP° CḡPēPSPsPe CḡC—PrPePs
PíPsPIC—PrPsPjP»CḡP»PsCíCḡ PīCḡPs PIPēPíP°PrPePē PSPμP°CḡC,PμCḡC—P°P»CḡPSPsC—
PíPμCḡPμPrPSCḡPsC— C—CēPμPjC—C†PSPsC— PSPμPICḡPsPíP°C,C—C— P·PsCḡPsPIPSPiPs
PSPμCḡPIP°, C%Ps C” PīCḡPēC†PēPSPsCḡ P·PSPēPḡPμPSPSCḡ P·PsCḡCí,
PIPeP»CḡC†P°CḡC†Pē PíPsCíC,C—PḡPSCí PIC,CḡP°C,Cí P·PsCḡCí, CḡPeC— P±CíP»Pē
PíPsPíBḡ™ CḡP·P°PSC— Cí C†P°CíC— C—P· P·P°CíC,PsCíCíPíP°PSPSCḡPj
C—PSPiC—P±C—C,PsCḡC—PI PαP”P°5, PIPeP»CḡC†P°CḡC†Pē CíPēP»PrPμPSP°C,,C—P». Pj
P±P°PíP°C,CḡPsC...B PíP°C†C—C”PSC,C—PI, P°P»Pμ PSPμ Cí PICíC—C..., P±CíP»Pē
PSP°CḡPIPSC— P°PSP°C,PsPjC—C†PSC— P°P±Ps CíCíPrPēPSPSC— C,,P°PeC,PsCḡPē CḡPēP·PēPeCí
CḡPsP·PIPēC,PeCí PSPμP°CḡC,PμCḡC—P°P»CḡPSPsC— PíPμCḡPμPrPSCḡPsC—
C—CēPμPjC—C†PSPsC— PSPμPICḡPsPíP°C,C—C— P·PsCḡPsPIPSPiPs PSPμCḡPIP°,
PIPeP»CḡC†P°CḡC†Pē (P°P»Pμ PSPμ PsP±PjPμPḡCíCḡC†PēCíCḡ) C,P°PeC—: PSPēP·CḡPePμ
CíPíC—PIPIC—PrPSPsCēPμPSPSCḡ PrC—P°PjPμC,CḡP° PμPeCíPeP°PIP°C†C—C— C,P° PrPēCíPeP°
P·PsCḡPsPIPSPiPs PSPμCḡPIP° (P·P°CíC,C—PḡPSPēPḡ PrPēCíPe P·PsCḡPsPIPSPiPs PSPμCḡPIP°),
PIC—Pe PíPsPSP°Pr 50 CḡPsPeC—PI, P°CḡC,PμCḡC—P°P»CḡPSP° PíC—PíPμCḡC,PμPSP·C—Cḡ,
P·P°C...PIPSPCḡPIP°PSPSCḡ PePsCḡPsPSP°CḡPSPēC... P°CḡC,PμCḡC—Pḡ,
PíC—PíPμCḡP»C—PíC—PrPμPjC—Cḡ C,P° PíP°P»C—PSPSCḡ. PkPμPjPsPḡP»PēPIPSP

PIPëP·PSP°C±PëC,Pë, C±Pë C†C- C‡PIPëC‰P° PïC‡C‡PjPs PïPsPIB‡™C‡P·P°PSC- C-P·
P·P°C‡C,PsC‡C†PIP°PSPSC‡Pj C-PSPiC-P±C-C,PsC‡C-PI PαP”P•5 C±Pë P· PSP°C‡PIPSPëPjPë
P°PSP°C,PsPjC-C±PSPëPjPë P°P±Ps C‡C†PrPëPSPSPëPjPë C,,P°PeC,PsC‡P°PjPë C‡PëP·PëPeC†,
C±Pë P· PePsPjP±C-PSP°C†C-C”C‡ C†PëC... PIC‡C-C... C,,P°PeC,PsC‡C-PI, C±Pë P· C-PSC€PëPjPë
C,,P°PeC,PsC‡P°PjPë.

P—PIC-C,C¿PIP°PSPSC‡ PïC‡Ps PïC-PrPsP·C‡C‡PIP°PSC- PïPsP±C-C±PSC- C‡PμP°PeC†C-C—.
P—PIC-C,C†PIP°PSPSC‡ PïC‡Ps PïC-PrPsP·C‡C‡PIP°PSC- PïPsP±C-C±PSC- C‡PμP°PeC†C-C—
PïC-C‡P»C‡ C‡PμC”C‡C,C‡P°C†C-C— P»C-PeP°C‡C‡C‡PePsPiPs P·P°C‡PsP±C† PjP°C”
PIP°P¶P»PëPIPμ P·PSP°C±PμPSPSC‡. P‡Pμ PrP°C” P·PjPsPiC† PïC‡PsPIPsPrPëC,Pë
P±PμP·PïPμC‡PμC‡PIPSPëPNë PjPsPSC-C,PsC‡PëPSPi C‡PïC-PIPIC-PrPSPsC€PμPSPSC‡
PePsC‡PëC‡C,C- C- C‡PëP·PëPeC-PI, PïPsPIB‡™C‡P·P°PSPëC... C-P·
P·P°C‡C,PsC‡C†PIP°PSPSC‡Pj C†C‡PsPiPs P»C-PeP°C‡C‡C‡PePsPiPs P·P°C‡PsP±C†.
P>C-PeP°C‡C‡Pj C‡P»C-Pr P·PIC-C,C†PIP°C,Pë PïC‡Ps P±C†PrC‡-C‡PeC-
PïC-PrPsP·C‡C‡PIP°PSC- PïPsP±C-C±PSC- C‡PμP°PeC†C-C— PIC-PrPïPsPIC-PrPSPs PrPs
PIPëPjPsPi P·P°PePsPSPsPrP°PIC‡C,PIP°.

PŷPμC‡PjC-PS PïC‡PëPrP°C,PSPsC‡C,C-. 3 C‡PsPePë.

PJPjPsPIPë P·P±PμC‡C-PiP°PSPSC‡.

P—P±PμC‡C-PiP°C,Pë PïC‡Pë C,PμPjPïPμC‡P°C,C†C‡C- PSPμ PIPëC‰Pμ 25 B°Pŷ.

P—P±PμC‡C-PiP°C,Pë C† PSPμPrPsC‡C,C†PïPSPsPjC† PrP»C‡ PrC-C,PμPNë PjC-C‡C†C-.

PJPïP°PePsPIPeP°.

PμPs 1 P°P±Ps 4 C,P°P±P»PμC,PePë C† P±P»C-C‡C,PμC‡C-. PμPs PsPrPSPsPjC†
P±P»C-C‡C,PμC‡C† C† PeP°C‡C,PsPSPSC-PNë PïP°C±C†C-.

PŷP°C,PμPiPsC‡C-C‡ PIC-PrPïC†C‡PeC†.

P—P° C‡PμC†PμPïC,PsPj.

P’PëC‡PsP±PSPëPe.

P’PμP»C†PïPs, P»C-PePë C,P° PePsC‡PjPμC,PëPeP°, Pr.Pr.

**PŷC-C‡C†PμP·PSP°C...PsPrP¶PμPSPSC‡ PIPëC‡PsP±PSPëPeP° C,P° P°PrC‡PμC‡P°
PjC-C‡C†C‡ PïC‡PsPIP°PrP¶PμPSPSC‡ PNëPsPiPs PrC-C‡P»C‡PSPsC‡C,C-.**

P’C†P». P”P°PSC-C†P° 5, 48000 PŷPsPïC‡PëPIPSPëC†C‡, P‡PsC‡PIP°C,C-C‡.